The New England
Journal of Medicine

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Volume 235 AUGUST 15, 1946 Number 7

# SCLEREDEMA: A SYSTEMIC DISEASE*

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BOSTON

IN 1900, Buschke[1] described the case of a forty-six-year-old carriage painter who suffered from persistent brawny induration of the skin of the face, chest and upper extremities. Following influenza, firm, nonpitting edema started in the neck and spread centrifugally. There was marked chemosis. The patient did not appear ill, had lost no weight, had no fever and had no complaints other than immobility of the skin. Buschke thought this picture to be distinct from those of previously reported syndromes and called the disease "scleredema adultorum."

Many papers have since appeared in Germany delineating and expanding the original concepts,[2–29] and a few reports were published in other European countries in the following thirty years,[30–35] but it was not until 1932 that the first note appeared in this country, when Epstein[36] reported 2 cases and reviewed the 41 cases previously described. Since then many publications have appeared,[37–75] and the disease is readily recognized. The 4 patients to be described herein were all observed at Mount Sinai Hospital within the last six years.

## CASE REPORTS

CASE 1 (M. S. H. 454642 and 472542). A 35-year-old German was admitted on April 3, 1940, 11 weeks following a sore throat and tonsillitis with elevation of temperature that lasted a few days. Four weeks after the onset of sore throat, the patient noted thickening and tightening of the skin of the back of the neck, which gradually spread to involve the trunk, arms and upper abdomen. Intravenous typhoid vaccine and short-wave and calcium therapy were without benefit.

Physical examination revealed a well-developed man with masklike, oily facies. Both eyelids were puffy. There was slight restriction in opening of the jaws and protrusion of the tongue. The blood pressure was 120/80. The skin felt strikingly inelastic, thick, indurated and bound down to the underlying tissue over the face, chest, neck, back, abdomen and upper extremities. The hands were minimally involved, and the lower extremities were normal.

The urine was normal and had a specific gravity of 1.031. A blood Wassermann test was negative. The blood urea nitrogen was 10 mg. per 100 cc., the sugar 80 mg., the cholesterol 280 mg., the cholesterol esters 165 mg., the phosphorus 3.8 mg., the calcium 11.2 mg., the total protein 6.5 per cent, and the creatinin 2.8 mg. A creatinin tolerance test showed no significant change. The basal metabolic rate ranged from −11 to −39 per cent. X-ray examinations of the chest, neck and skull were negative. Electrocardiographic tracings showed low voltage and an inverted $T_4$. Biopsy of the skin over the deltoid region revealed no abnormality. The sugar-tolerance curves ranged from 75 to 95 mg. per 100 cc.

Desiccated thyroid was given in doses up to 0.7 gm. daily, but without benefit. Hyperthermia was tried, and the patient experienced loosening of the skin following each treatment for several hours, but there was no lasting relief.

The patient was discharged after 3 weeks and was observed in the Out Patient Department for 1 year. On April 29, 1941, he was readmitted to the hospital for further study. During this interval there were only minor fluctuations in the stiffness and induration of the skin.

The findings on readmission were essentially those of the first admission. The hemoglobin was 88 per cent (Sahli) and the white-cell count 9950, with a normal differential count. The basal metabolic rate on two occasions was −4 and −10 per cent. A test showed sweating to be markedly reduced over the entire body. The sugar-tolerance curve was normal. The chloride was 595 mg. per 100 cc., the alkaline phosphatase 10 K-A units, the albumin 5.1 gm., the globulin 1.6 gm., and the icteric index 6. The other blood chemical findings were essentially those during the first admission. Throat cultures revealed beta-hemolytic and alpha-hemolytic streptococci. The urine was negative, as were electrocardiographic tracings. A biopsy of the left deltoid region showed swelling of the collagen bundles of the corium and subcutaneous tissue. With *Kresylechtviolett* a faint pink-staining intercollagenous substance, such as that described by Freund,[12] was demonstrated. The histologic findings were interpreted as consistent with scleredema adultorum.

On the 13th hospital day, treatment with 3 cc. of dihydrotachysterol daily was begun, and after 2 days this dosage was increased to 5 cc. After 12 days of this therapy, the patient manifested severe toxic symptoms characterized by malaise and vomiting. The calcium blood level was 14.5 mg. per 100 cc. The skin seemed to have softened, although there had been no dramatic improvement. The patient was discharged at his own request after 2 months of hospitalization.

Follow-up examination in December, 1944, showed the skin of the upper extremities to be hard and inelastic. The masklike facial expression was still present, although the cutaneous changes of the thorax, abdomen and neck had disappeared.

CASE 2 (M. S. H., O.P.D. 40-4027). The patient, a 16-year-old Puerto Rican girl, had been in good health until April, 1940, when she developed pneumonia with subsequent empyema, necessitating surgical drainage. One month after recovery she developed sudden swelling of the back of the neck, face and scalp, with difficulty in moving the head from side to side. In a few days the swelling spread to involve the shoulders and upper arms.

Physical examination revealed a young girl with a hard edema in the areas previously described. The skin was taut, had a rubbery consistence and did not pit on pressure. There was no affection of the underlying muscles. The blood pres-

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sure was 120/80. The remainder of the physical examination was not remarkable.

The urine was normal. The hemoglobin was 85 per cent (Sahli) and the white-cell count 6300, with a normal differential count. A blood Wassermann test was negative. The blood urea nitrogen was 13 mg. per 100 cc., the sugar 75 mg., the calcium 10.6 mg., the phosphorus 4.0 mg., and the alkaline phosphatase 9 K-A units. The sedimentation rate of erythrocytes was not increased. The basal metabolic rate was +8 per cent. An electrocardiogram showed low voltage of the QRS complexes.

The patient was followed for 3 years in the Out Patient Department. She was given numerous hyperthermia treatments and felt considerably improved after each treatment. The swelling gradually receded but was still marked when the patient was last seen 3 years after the onset of the illness.

CASE 3 (M. S. H. 519043 and 525942). A 37-year-old woman was admitted on April 14, 1944, about 8 weeks after the onset of edema of the face and neck. One month before the onset of these complaints all the teeth had been extracted. The extractions were followed by severe infection of the sockets, lasting for 1 week. Three weeks later edema of the neck, face and breasts developed, spreading to the back, chest and lower extremities. The upper extremities were never involved. The edema was unsightly but not discomforting. The patient was otherwise in good health.

Physical examination revealed edema of the face, conjunctivas, trunk, abdomen and lower extremities. The edema was remarkable in that it was firm and pale and did not pit on pressure. It was not dependent in location and had no relation to gravity, and there was no change in the course of the day. The edema was most marked about the face, especially the forehead, and was present to a moderate degree over the areas previously enumerated. There were marked chemosis and considerable lacrimation. The heart and lungs were not remarkable. The blood pressure was 110/90. A soft liver edge was felt approximately 1 cm. below the costal margin. Neurologic examination was not remarkable.

Repeated urine examinations showed no protein or formed elements. The hemoglobin was 85 per cent (Sahli) and the white-cell count 4900, with a normal differential count. The erythrocyte sedimentation rate was 72 minutes. The venous pressure was 7 cm., and the circulation time (decholin) was 17 seconds. The basal metabolic rate was −6, −9 and −3 per cent. Repeated stool examinations revealed no parasites or occult blood. Phenolsulfonphthalein tests on two occasions showed 35 and 25 per cent excretion in 1 hour. The concentration test showed a maximal specific gravity of 1.030. A galactose-tolerance test showed an excretion of 0.85 gm. An oral hippuric acid test revealed an excretion of 3.8 gm. The initial total protein was 6.0 gm. per 100 cc., and subsequent determinations were within normal limits. The albumin was 3.7 gm., the globulin 2.3 gm., the phosphorus 4 mg., the calcium 10 mg., the chloride 640 mg., and the cholesterol 300 mg. per 100 cc. A bromsulfalein test showed no significant retention.

X-ray examination of the chest revealed an effusion occupying the lower portion of each pleural cavity. The size of the heart could not be determined. A flat plate of the abdomen showed general density, suggesting fluid. A number of electrocardiographic tracings revealed a regular sinus rhythm, with QRS complexes and T waves of extremely low voltage. A skin test for trichinosis was negative.

During the first 3 weeks in the hospital, the urinary output was high, but there was a gain in weight from 165 to 173 pounds. The patient was given injections of Mercupurin, which were effective in producing loss of weight. Nevertheless she remained quite edematous and 15 pounds above her usual weight. Desiccated thyroid was given in large doses, without result, although the basal metabolic rate rose to +9 per cent. Large amounts of human plasma were finally administered without significant effect. The patient was discharged essentially unimproved after 3 months of hospitalization, to return 3 months later for further study. During the interim the edema remained constant. She was readmitted on October 5, 1944.

Physical examination on readmission showed marked edema of the eyelids and conjunctivas. The skin over the previously mentioned areas was edematous and hard, although mostly over the breasts and back. It could not be lifted from the underlying structures, although there was no atrophy or pigmentation. There were many striae but no scarring over the back and abdomen. The lungs and heart were not remarkable. The blood pressure was 110/70. The hemoglobin was 72 per cent (Sahli) and the white-cell count 5700, with a normal differential count. Urine examinations were always normal. The blood urea nitrogen was 17 mg. per 100 cc., the total protein 6 gm., with an albumin of 3.9 gm. and a globulin of 1.9 gm., the phosphorus 3 mg., the calcium 10.9 mg., the cholesterol 240 mg., the sodium 143.2 milliequiv. per liter, the chloride 104.2 milliequiv., and the uric acid 3.6 mg. per 100 cc. A blood Wassermann test was negative. The antifibrinolysin titer was zero. The Aschheim–Zondek test was negative. The visual fields were within normal limits. The basal metabolic rate was −2 per cent. Repeated Sulkowitch tests on the urine gave reactions within normal limits. Skin sensitivity to ultraviolet light was normal. Hippuric acid, phenolsulfonphthalein and cephalin-flocculation tests were negative. A creatin-tolerance test was negative. Calcium excretion of a 3-day urine specimen of 2635 cc. following a Bauer–Aub diet showed 230 mg. calcium excretion, which is normal. A salt-tolerance test was negative. Two 17-ketosteroid determinations were 12.0 and 16.6 mg. per 100 cc., respectively, which are normal. The blood-iodine level was 5 gamma, which is normal. The sedimentation rate of erythrocytes was repeatedly normal.

X-ray examination of the chest showed enlargement of the cardiac shadow to the right and left. There was an enlargement of the right border with markedly diminished pulsation by fluoroscopy and kymography, suggesting a localized pericardial effusion. Right and left pleural effusions that had previously been present had disappeared. Examination of the long bones showed no abnormality. Examination of the sella turcica was negative. Electrocardiographic tracings showed a regular sinus rhythm, left-axis deviation and QRS of low voltage, changes seen in pericardial effusion.

A biopsy of the skin of the right breast showed changes compatible with the diagnosis of scleredema adultorum. Staining with *Kresylechtviolett*, however, did not reveal an intercollagenous substance.

The patient's course was uneventful except for purulent conjunctivitis, the etiology of which was not discovered. Slitlamp examination of the cornea revealed no abnormality. The temperature was normal throughout. There was both subjective and objective improvement. She was treated with effervescent urea, from which she had a good diuresis, but after 2 weeks of its use she became refractory to it and her weight became stabilized at 134 pounds. Because of previously reported pituitary disturbances in scleredema adultorum,[23,25,33,65] anterior-pituitary extract (Ambinone) was given every 2nd day in 1-cc. doses. The weight subsequently fell from 134 to 128 pounds, while the fluid intake remained restricted throughout. The skin softened noticeably, and the patient was discharged at her own request. The injections were continued three times weekly for 3 months following discharge.

When the patient was last seen in July, 1945, all the skin lesions had disappeared, x-ray examination of the chest was negative, and save for some residual chemosis there was no evidence of the previous disorder.

CASE 4 (M. S. H. 535256). The patient, a 33-year-old woman, was first admitted on June 4, 1945. She had been well until the summer of 1943, when she developed generalized, hard, brawny edema of the neck, face, abdominal wall, vulva, thighs and legs but not of the upper extremities and chest. A biopsy specimen was taken from the buttocks and was reported as scleroderma. The urine was said to contain formed elements and erythrocytes on several occasions during the early stages of her illness, but subsequently all examinations were negative and renal function was normal throughout. Bilateral pleural effusions developed and required continuous tapping for more than 9 months. Oliguria was an outstanding symptom. There was no cardiovascular disease. The patient was seen by various consultants in different hospitals over the course of 2 years, but no definite diagnosis could be arrived at. The blood chemical values, particularly the total protein, albumin and globulin determinations, were within normal limits at all times. The patient was given all types of available diuretics, without any therapeutic success. Among other measures autoinfusion with pleural fluid and renal decapsulation were performed, without benefit. The generalized edema slowly disappeared over the course of months, although the patient was left with residual brawny edema of the face, conjunctivas, eyelids and

legs. The skin of the feet was spared. There was no pigmentation of the skin or scarring anywhere.

On physical examination the eyelids were markedly puffy and distorted the face, which was mildly edematous. The conjunctivas were swollen and edematous. The upper respiratory passages, heart, lungs and abdomen were normal, and neurologic examination was not remarkable. There was hard, nonpitting edema of the legs and thighs. No pigmentation or scarring was present. The feet were spared. There was no sacral edema. The hemoglobin was 70 per cent (Sahli), the red-cell count 3,900,000, and the white-cell count 5000, with a normal differential count. The urine was repeatedly negative, as was the blood Wassermann reaction. The blood urea nitrogen was 8 mg. per 100 cc., the sugar 75 mg., the chloride 595 mg., the cholesterol 292 mg., the cholesterol esters 205 mg., the carbon dioxide combining power 51 vol. per cent, the phosphorus 3.4 mg. per 100 cc., the calcium 9.5 mg., and the total protein 6.7 gm., with an albumin of 3.8 gm. and a globulin of 2.9 gm. The hippuric acid excretion was 6 gm., and the galactose excretion 1.5 gm. An electrocardiogram revealed no abnormality. An electroencephalogram was negative. X-ray examination of the skull was negative. X-ray examination of the chest revealed no abnormality of the lungs or pleural cavities. Fluoroscopy showed the border of the right heart to be prominent with diminished pulsations, a fact that was confirmed by kymography. Intravenous pyelography revealed slight ptosis of the kidneys. There was no demonstrable abnormality in the urinary tract. The basal metabolic rate was +11 per cent. The sedimentation rate of erythrocytes was 29 mm. per hour. A skin test for trichinous infection was negative. A biopsy specimen taken from the leg showed nothing significant. A urine concentration test gave a specific gravity of 1.030, and phenolsulfonphthalein excretion was normal.

The patient had been admitted for diagnostic purposes. She was afebrile on entry and there was no significant change in her condition during her stay. No treatment was administered. The disease process was considered to be scleredema adultorum, and the ultimate prognosis was thought to be good. She was discharged after 3 weeks of hospitalization.

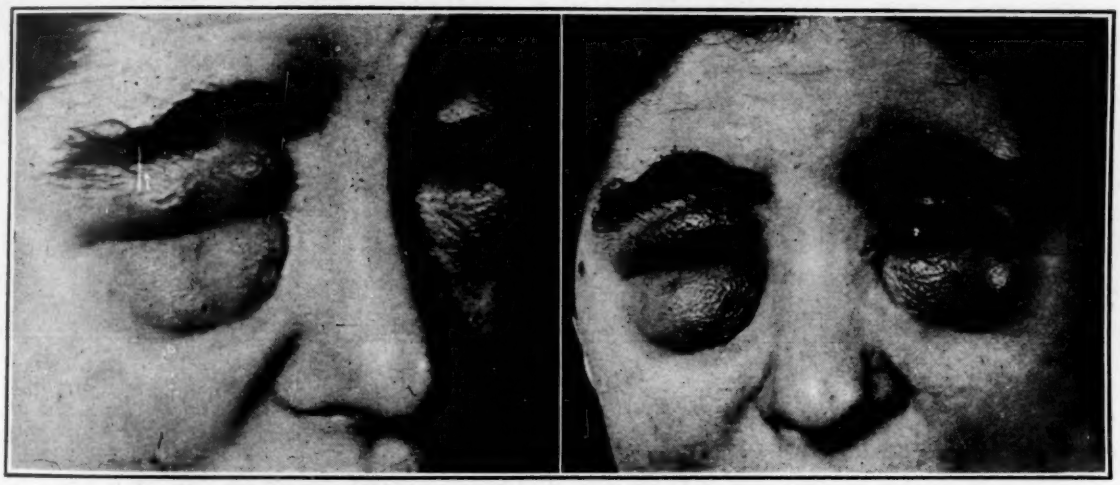


FIGURE 1. *Case 4.*
*These photographs were taken in June, 1945. Note the marked eyelid changes and chemosis.*

## CLINICAL MANIFESTATIONS

In most of these cases of scleredema a febrile illness preceded the onset of the disorder. The infections have most frequently been influenza, sore throat, tonsillitis and scarlet fever. It is interesting to note that in most cases the initial illness has been streptococcal in origin. This acute infection disappears and the patient enters an asymptomatic period varying from several days to as long as three months. The onset of the edema may be the initial manifestation of scleredema, or there may be a short prodromal period of malaise, myalgia and even low-grade temperature.

The appearance of a patient with scleredema is so striking as to suggest the diagnosis immediately. The face, neck, thorax, legs and buttocks present an extensive pale swelling. The normal mobility of the face is lost. The lines are obliterated by a dull, waxy swelling. The lack of facial expression suggests the masklike facies of parkinsonism. The conjunctivas are thickened and elevated, but the edema ends abruptly at the cornea. The eyelids are especially involved (Fig. 1), frequently being swollen and red. The pallor of the edema is so pronounced that patients are often thought to be anemic, although the dead-white color of scleroderma is lacking. The edema is hard and nonpitting. On palpation the skin and subcutaneous tissue feel thickened and indurated. The affected skin cannot be picked up in folds or creased. Occasionally an erythematous or scaly rash affecting the arms and face is transiently present. Closer examination of the affected areas reveals that the normal pits and skin markings are well preserved or exaggerated. The dermal appendages are not affected.

Scleredema most frequently begins in the nape of the neck and spreads to the face, thorax and shoulders. Not infrequently the abdomen, lower and upper extremities and buttocks are involved. More rarely the tongue and pharyngeal tissues are affected.[29, 36, 42] The tongue is described as immobile and large, the patient suffering from dysarthria. Complaints of dysphagia are referred to scleredema of the pharynx. Several observers have noted that

the scleredema frequently begins in that area, which has been affected by the previous febrile illness. It is a characteristic feature of the disease that the hands and feet are spared.

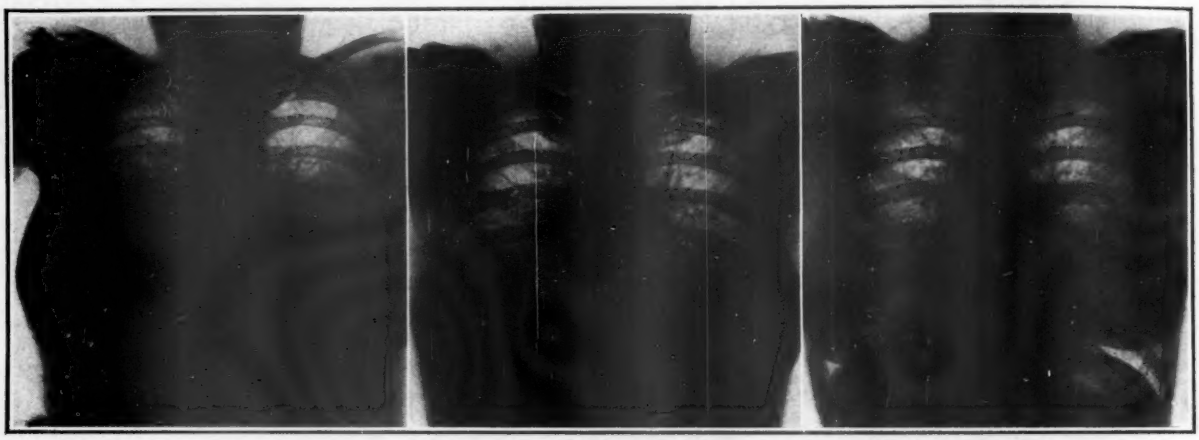
The skin is not the only system affected. Cases 3 and 4 showed hydrothorax, and hydrarthrosis was found by Voss,[28] Schnitzer,[63] and O'Leary.[57] The patient's complaints usually relate either to the facial edema or to the immobility of the skin. Not infrequently the stiffening of the skin of the thorax restricts chest motion,[22] producing a sensation of dyspnea. Occasionally movements of the extremities are hampered. The maximal area of skin involvement is reached early in the disease, and the course thereafter is one of slow regression. Regression usually begins in the areas last affected and persists longest in those first involved, particularly the neck, face and scalp. Complete resolution has occurred in few cases in less than a month.[17, 29] In most cases regression takes longer than six months, and not infrequently islands of scleredema are left, slowly resolving after a period of years. It is frequently stated that the disease is self-limited, but the case reported by Adler[2] showed evidence of scleredema of the eyelids after twenty years. In the case described by Hoffmann,[15] extensive edema persisted for fifteen years. The prognosis for life and function is excellent, and ultimate complete recovery can be expected, yet the duration of the edema is unpredictable.

In a number of cases relapses have occurred.[2, 3, 36, 57] These characteristically occur after a long free period, — thirteen years in Epstein's[36] patients and twenty years in one of O'Leary.[57]

Except in a few cases in which the initiating febrile illness was nephritis,[13, 19, 45, 52, 63] the urine consistently shows no abnormality. The total urinary output has not often been recorded, but Buschke[9] noted that during the edematous phase there was oliguria; with regression of the edema he observed marked diuresis.

The blood is usually within normal limits, showing neither anemia nor leukocytosis. The sedimentation rate is normal or at best slightly elevated.

The basal metabolic rate has been reported as being high[61–63] and as being low.[45] In most cases, however, it is in the normal range, as in the present series.



A B C

FIGURE 2. *Roentgenograms in Case 3.*

A — *This film was taken on admission in April, 1944.* B — *This film was taken during second admission and shows disappearance of the pleural effusion but persistence of the pericardial effusion, particularly prominent at the right pericardial border.* C — *This film was taken in June, 1945, when the resolution of the cutaneous manifestations was virtually complete. The patient never had clinical symptoms referable to intrathoracic effusions.*

In these cases the total protein, albumin, globulin, chloride, glucose-tolerance, blood-sugar, calcium and phosphorus levels were normal. The 17-ketosteroid excretion in Case 3 was normal, as was the blood-iodine level. No significant blood chemical aberrations have been noted by other authors.[37, 43, 57, 60, 63]

Electrocardiograms showed QRS complexes of low voltage.

X-ray examination of the chest has only rarely been included in clinical reports but usually shows no abnormality. Nevertheless, the patient in Case 3 had a right pleural effusion when first seen and later developed a loculated effusion along the right border of the heart. Both these effusions regressed as the process cleared up. In Case 4, there were massive bilateral pleural effusions during the initial phase of the disease (Fig. 2). To our knowledge, these are the first cases in which pleural and pericardial effusions have been reported as part of the

scleredema syndrome. Such intrathoracic effusions we believe to be intrinsic features of the disease. This indicates, as do the reported hydrarthroses, that scleredema is not limited to the skin and subcutaneous tissue and may in fact present a puzzling picture to the internist.

## Incidence

In 1937, Touraine, Golé and Soulignac[70] were able to collect 70 cases from the literature. We have found a total of 99 reported cases and add 4 of our own, bringing the total to 103. In 97 cases in which knowledge of the sex is available, the patients were men in 33 and women in 64, an incidence of almost two to one in favor of women. An identical ratio is reported by Touraine et al.[70] The greatest age incidence is in childhood and early adult life, as shown in Table 1. The oldest patient reported was

Table 1. *Age Incidence.*

| Age | No. of Cases |
|---|---|
| yr. | |
| 10 and less | 27 |
| 11-20 | 22 |
| 21-30 | 18 |
| 31-40 | 12 |
| 41-50 | 10 |
| 51-60 | 6 |
| 61 and over | 3 |

sixty-eight years old.[30] The disease has also been observed in the early neonatal period.[11, 17]

## Pathology

The squamous-cell and keratin layers of the epidermis present no abnormalities. The basal-cell layer may be alternately flattened out or heaped up. The superficial layers of the cutis usually show no feature other than slight perivascular infiltration.[12] Epstein[36] noted a band of connective tissue underlying the epidermis. The infiltrating cells are usually fibroblasts, lymphocytes and plasma cells.

The characteristic pathologic features are found in the deeper layers of the cutis.[12] The perivascular infiltration is more pronounced here, although it is variable and may not be at all striking. The collagen bundles are thickened to several times their usual diameter and form a firm fibrous band. Separating the collagen bundles and in interstitial areas throughout the cutis and subcutis are clear areas. There are also areas of fenestration about the blood vessels and hair follicles. With haematoxylin-eosin stain these areas appear empty. Freund[12] used *Kresylechtviolett*, which stained the tissues blue-gray but the material in these clear spaces a brilliant red. He also demonstrated small patches of this amorphous material in islands throughout the entire cutis. Both Voss[28] and O'Leary,[57] however, were unable to stain the interstitial material with *Kresylechtviolett*. This dye in one of our cases also failed to stain the clear areas, and in another case it was only partially satisfactory. This apparent discrepancy is explained by the fact that the microscopic picture is variable. It probably varies with the stage of the disease, as noted by Epstein,[36] and may vary in different areas, retaining, however, the three major characteristics of perivascular infiltration, swelling of the collagen bundles and the presence of areas of fenestration.

The only autopsied case is that of Stenbeck.[65] He describes proliferation of connective tissue throughout the entire body, leading eventually to death through strangulation of the bowel. This patient, however, presented many unusual features, and the case cannot be accepted as an established one of scleredema.

## Etiology

Buschke[1] was vague about the etiology in his first case. He suggested that the initial infection injured the lymph channels, producing elephantiasis of the skin. That the initial infection produces the agent responsible for the disease is the opinion of many contributors. Credence is lent to this thesis by the fact that the initiating infection is most frequently streptococcal in nature (Table 2). In addition, in a number of cases the area of scleredema began in the region of the skin injured by the infection.[22, 27, 30, 32] Guy[45] noted in 1 case that skin sensitivity tests for streptococci were markedly positive.

Table 2. *Preceding Infections.*

| Disease | No. of Cases |
|---|---|
| Influenza | 24 |
| Sore throat | 9 |
| Scarlet fever | 8 |
| Tonsillitis | 6 |
| Nephritis | 6 |
| Rheumatic fever | 3 |
| Respiratory infection | 3 |
| Fever | 3 |
| Pneumonia | 2 |
| Encephalitis | 2 |
| Pyoderma | 2 |
| Measles | 2 |
| Abortion | 2 |
| Wound infection | 1 |
| Dental infection | 2 |
| Otitis media | 1 |
| Erysipelas | 1 |
| Mumps | 1 |
| Typhus fever | 1 |
| No preceding infection | 5 |

There is some evidence pointing to the endocrine organs as possible causative factors. No persistent changes in the basal metabolic rate have been described, but in a few cases x-ray evidence of tumor of the pituitary was evident.[12, 25, 53, 65] In one of these cases, which showed enlargement of the pituitary bed and destruction of the posterior clinoid processes, Schreus[25] claims to have experimentally demonstrated a substance in the blood and urine having the same effect on water metabolism as does the extract of the posterior pituitary gland. Selye[76]

thinks that topical application of estrogens in mice produces a pathologic picture resembling that of scleredema.

Helfand,[46] struck by the clinical resemblance between trophedema and scleredema, suggested that the pathogenesis might be disease of the peripheral nerves. He demonstrated with Spielmeyer and Weigert–Pal stains disintegration of the myelin sheaths of the subcutaneous nerve fibers.

At present, however, there is insufficient material available to permit a reasonable opinion of the etiology.

## Differential Diagnosis

There are few cases of scleredema that have not at one time been diagnosed as scleroderma, but the differentiation may be easily made on clinical grounds. The hands, so frequently diseased in scleroderma, are spared in scleredema. The skin similarly does not show the atrophy and contractures or areas of pigmentation and depigmentation seen in scleroderma. Whereas scleroderma frequently produces disease of the lungs, esophagus and heart and decalcification of the bones, these changes are never seen in scleredema. Finally, scleredema is a benign and self-limited disease and is usually seen in the stage of regression.

Myxedema may be differentiated by means of the basal metabolic rate, the blood cholesterol values, the general appearance and behavior of the patient and finally the lack of response to desiccated thyroid.

Dermatomyositis occasionally gives rise to a difficult diagnostic problem. Touraine et al.[70–72] claim that a number of cases described as acute dermatomyositis are actually scleredema. Nevertheless. the presence of muscle pain, fever, a high sedimentation rate and the widespread erythematous skin lesions occasionally seen in dermatomyositis and the weakness and atrophy that are constant features of the disease are not seen in scleredema. Finally, dermatomyositis is usually a progressive and crippling disease. Recovery, which is not frequent, is attended by atrophy and incapacity.

Trichinosis may be ruled out on the basis of the elevation of temperature, the marked muscle tenderness, eosinophilia and the localization and nature of the edema. The skin and complement-fixation tests serve as laboratory aids in the differential diagnosis.

Edema from cardiac and renal as well as hepatic disease is readily differentiated by simple clinical grounds.

## Treatment

The treatment of the disease is unsatisfactory. The disease appears to follow its own course, unaffected by any therapeutic agents. Our therapeutic trials included desiccated thyroid, dihydrotachysterol and anterior pituitary extract. These agents did not contribute markedly to the patients' recovery. O'Leary[57] claims beneficial results from fever therapy, but his results with it, as well as our own, are not striking. It is also doubtful whether eradication of a focus of infection can be expected to influence the course of the disease. Further studies of the pathogenesis of the process may elucidate the therapeutic problem.

## Discussion

The name "scleredema adultorum," as given by Buschke,[1] does not seem appropriate. The term implies that this is an illness seen only in adults; yet the statistics on age distribution (Table 1) show that it is most frequently observed in children and adolescents, who account for 50 per cent of all cases on record. Calling the disease "scleredema" without reference to the age groups affected seems more in keeping with the statistical facts.

The recognition of the disease is important because of the excellent prognosis for function and life. The process always undergoes spontaneous regression, in contrast to scleroderma and dermatomyositis, with which it is frequently confused. The pleural effusions in 2 of our cases and the electrocardiographic changes are of interest, particularly since the intrathoracic effusions receded simultaneously with improvement of the cutaneous changes.

Cases of scleredema undoubtedly come under the observation of internists. A relatively small number of cases have been reported in the literature to date. Nevertheless, we have observed and followed 4 cases ourselves within a relatively short period. It seems to be a reasonable conclusion that the disease is not so infrequent as might be suspected.

Any case presenting obscure forms of edema should be suspected, and a detailed history may aid in ascertaining its true cause.

## Summary

Scleredema was first described by Buschke. Since his original description 99 cases have appeared in the literature, to which we add 4.

The disease is characterized by firm, nonpitting edema, affecting usually the face, neck, scalp, conjunctivas, thorax, occasionally the arms and more rarely the legs, sparing the hands and feet. Pleural effusions, pericardial effusions and hydrarthroses also occur. The pericardial effusions may be localized. The electrocardiogram shows low voltage of the QRS complexes.

Complete recovery can be expected over a period varying from several months to many years.

Young people are affected more frequently than those in the older age groups. Women are affected twice as often as men.

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# SOME UNUSUAL FINDINGS IN AN EPIDEMIC OF ANTERIOR POLIOMYELITIS*

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DURING the months of March and April, 1945, a southern army post experienced a short but explosive outbreak of anterior poliomyelitis. Within a period of twenty-five days, 18 patients suffering from poliomyelitis were admitted to the hospital. There were 3 other cases that were considered to be preparalytic in type, but since the diagnosis was questionable, they are omitted from this discussion.

Anterior poliomyelitis is usually a disease of late summer and early fall. Winter epidemics have been described, but this outbreak cannot be so classified. The weather was unusually warm for the time of year, even though it is taken into consideration that the camp is situated in the southern part of the country; indeed, the temperatures approached those occurring in the summertime.

The diagnosis of acute poliomyelitis was confirmed by pathological studies, autopsies being performed in the 3 fatal cases. Histologic sections of the spinal cord and medulla revealed lesions characteristic of anterior poliomyelitis. Also, poliomyelitic virus was recovered from the central nervous system of 1 of the patients.*

All the cases occurred in soldiers, whose ages ranged from eighteen to thirty-three years; all but 3 were between eighteen and twenty-one years old. This camp has approximately 30,000 troops, most of whom are recruits, largely infantrymen. Some of those who contracted the disease lived outside the camp, although the great majority were stationed on the post. The post is located four miles from a city with a population of 40,000, and traffic between the camp and city is extensive. In spite of this, no cases occurred in any of the civilian population. It is not the purpose of this paper to discuss any epidemiologic aspect of this outbreak, but it should be stated that there was no personal contact between any of the patients.

The patients afflicted with the disease in this epidemic showed some unusual findings. There were 10 (55 per cent) with bulbar involvement. There were 3 deaths, all in cases with bulbar involvement and all caused by failure of the respiratory center. Also of considerable interest were some unusual spinal-fluid findings. This subject is discussed in detail below.

In Table 1 are detailed the symptoms and their frequency of occurrence. As can be seen, headache was the symptom most commonly noted, but in no case was it severe or marked, nor was it the chief complaint in any case. In a few cases direct questioning was necessary to elicit this symptom. Muscle pain, backache and dysphagia were the next most frequent symptoms. The muscle pain was described in the majority of cases as "soreness" or "aches," and in some cases as an acute, severe pain. There were no shooting pains, such as those experienced in radiculitis. Dysphagia varied in intensity. Some patients were completely unable to swallow; others were able to swallow small amounts of liquids and soft, mushy foods, generally washed down with liquids. Those who were able to swallow liquids tired easily, and it required an appreciable effort for them to swallow. The listing of stiffness of the neck as a symptom refers to subjective stiffness as reported by the patients, not to objective findings of stiffness, which were much more frequent (Table 2).

TABLE 1. *Symptoms.*

| SYMPTOMS | No. of CASES |
|---|---|
| Headache | 12 |
| Muscle pain | 11 |
| Backache | 10 |
| Dysphagia | 10 |
| Nausea and vomiting | 6 |
| Voice change | 5 |
| Muscle weakness | 5 |
| Fever | 5 |
| Chilliness | 3 |
| Sore throat | 3 |
| Abdominal pain | 1 |

The physical findings have been divided into two groups, those in cases with bulbar involvement and those without it. Cranial nerves were affected in all bulbar cases, and paralysis of the extremities occurred in certain cases of both groups. The latter was generally mild. Of the cases with bulbar involvement, 5 showed no evidence of actual paralysis, but in 4 of these there was peripheral muscle weakness. The patient who showed no evidence of cord involvement died within a week after the onset of his illness.

TABLE 2. *Physical Findings.*

| FINDING | No. of CASES |
|---|---|
| Cases with bulbar involvement: | |
| Fever | 10 |
| Uvula paralysis | 10 |
| Muscle tenderness | 10 |
| Stiff neck | 8 |
| Paralysis of muscles of the extremities | 5 |
| Facial paralysis | 4 |
| Weakness of muscles of the extremities | 4 |
| Weakness of sternomastoid muscle | 1 |
| Injected pharynx | 1 |
| Weakness of muscles of jaw | 1 |
| Cases without bulbar involvement: | |
| Weakness of muscles of the extremities | 8 |
| Fever | 7 |
| Paralysis of muscles of the extremities | 7 |
| Muscle tenderness | 6 |
| Stiff neck | 4 |
| Injected pharynx | 2 |

*This work was done by the Commission on Neurotropic Virus Diseases, Office of the Surgeon General, United States Army.

Muscle tenderness was present in all the cases with bulbar involvement and in 6 of those without it, a total of 16 cases. The muscle groups in which tenderness was found, in the order of frequency, were the hamstring muscles, the posterior calf muscles, the quadriceps muscles and the biceps muscles. It was interesting that tenderness of the muscles of the upper extremities was found in only 2 cases, although paralysis of the upper extremities occurred in 9 patients. One of the 2 patients without muscle tenderness was admitted three and a half weeks after the onset of his illness, and the other showed only involvement of the upper extremities, primarily the abductor muscles of the shoulders. It was also of interest that many more patients showed muscle tenderness than complained of muscle soreness. The tenderness persisted from a few days to weeks.

Fever was present in all cases but 1, which was that of the patient who entered the hospital late in the course of his disease. The height and length of the fever was variable. The temperatures generally ran from 100 to 103°F., but in 3 of the bulbar-involvement cases it was 104°F. Death occurred in 2 of these. So long as the temperature remains elevated, one cannot be certain how much more progression of the disease process there will be. In the bulbar-involvement cases this factor was of prognostic significance.

Muscle spasm was seen in no case with the patient at complete rest. There was no attempt to study muscle spasm by means of the electromyograph or by chronaxie measurements, so that any evidence of muscle spasm was that judged on a purely clinical basis. When certain muscles were placed on stretch, pain and spasm were generally elicited, their principal locations being the neck, back, hamstring muscles and posterior calf muscles. They were not, however, always elicited in paralyzed muscles. In the cases in which the tibialis anticus muscle and the abductor muscles of the shoulder were involved, passive stretching produced neither spasm nor pain. As pointed out by Moldaver,[1] muscle spasm in anterior poliomyelitis is a complex phenomenon, the result of a combination of factors — namely, a normal stretch reflex, meningeal irritation of the posterior roots, an increase of normal tonus in healthy and strong muscles or muscular fibers opposed to weak or paralyzed muscles, and lesions of the dorsal-root ganglions and posterior horns.

Reflex changes were not listed because of their variability and changeability. In most cases with complete muscle paralysis deep reflexes were absent in the involved area, but 1 of the cases with extensive paralysis showed hyperactive deep reflexes throughout. In another case with fairly extensive involvement there were no reflex changes. The reflexes in the same patient often varied from day to day. This was particularly true in the patients with muscle tenderness and weakness but no residual paralysis. As the muscle tenderness disappeared and strength returned, the reflexes became normal. No pathologic reflexes were obtained. There was no evidence of cortical involvement in any patient.

Sensory changes were elicited in only 1 patient. A summary of this case is given below.

The spinal-fluid findings are listed in Table 3. Only the cell counts and total proteins are recorded. Sugar determinations and Wassermann reactions are omitted, since the former were either within normal limits or slightly elevated and all the latter were negative. The day of withdrawal of the spinal fluid and its examination is recorded in terms of the onset of the disease.

TABLE 3. *Spinal-Fluid Findings.*

| No. of Case | Cell Count: Total Cells | Cell Count: Polymorphonuclear Cells | Cell Count: Lymphocytes | Total Protein | Day of Illness |
|---|---|---|---|---|---|
| | | | | *mg./100 cc.* | |
| **Cases with bulbar involvement:** | | | | | |
| 1 | 495 | 470 | 25 | 65 | 4 |
| 2 | 9 | 2 | 7 | 48 | 3 |
| | 10 | 0 | 10 | 48 | 5 |
| 3 | 0 | 0 | 0 | 74 | 7 |
| | 10 | 0 | 10 | 74 | 9 |
| 4 | 14 | 0 | 14 | 31 | 5 |
| | 14 | 0 | 14 | 31 | 8 |
| 5 | 5 | 0 | 5 | 67 | 4 |
| | 22 | 1 | 21 | 43 | 7 |
| 6 | 1 | 0 | 1 | 20 | 4 |
| | 0 | 0 | 0 | 15 | 8 |
| | 0 | 0 | 0 | 20 | 21 |
| 7 | 9 | 2 | 7 | 33 | 5 |
| | 25 | 1 | 24 | 48 | 10 |
| 8 | 400 | 72 | 328 | 47 | 4 |
| 9 | 5 | 1 | 4 | 54 | 5 |
| | 13 | 4 | 9 | 105 | 15 |
| 10 | 5 | 2 | 3 | 50 | 3 |
| | 3 | 0 | 3 | 150 | 10 |
| | 1 | 0 | 1 | 270 | 28 |
| **Cases without bulbar involvement:** | | | | | |
| 11 | 21 | 0 | 21 | 43 | 5 |
| 12 | 110 | 15 | 95 | 14 | 7 |
| 13 | 85 | 10 | 75 | 43 | 5 |
| 14 | 2 | 0 | 2 | 44 | 25 |
| 15 | 2 | 0 | 2 | 48 | 3 |
| | 17 | 1 | 16 | 43 | 9 |
| 16 | 41 | 2 | 39 | 36 | 3 |
| 17 | 37 | 0 | 37 | 36 | 5 |
| 18 | 2 | 0 | 2 | 43 | 4 |
| | 3 | 0 | 3 | 37 | 10 |
| | 0 | 0 | 0 | 39 | 20 |
| | 1 | 0 | 1 | 39 | 32 |
| | 1 | 0 | 1 | 39 | 42 |

In cases 1 and 8 differential expressed in percentages.

Repeat spinal-fluid examinations were done in all cases in which the first examination revealed a normal cell count. In 7 cases with bulbar involvement, the spinal fluid obtained on admission showed a normal cell count or one below 10. In the group without bulbar involvement, the initial spinal fluid was normal in 3. One of these patients, however, was admitted late in the course of his illness, and since normal cell counts are not unusual at that time, it was believed that this case should be omitted in the calculation of the percentage. The remaining spinal fluids were obtained from patients in the first week of their illness. Thus, 53 per cent of the spinal fluids obtained on admission showed essentially normal counts — in 7 of the cases with bulbar involvement

and in 2 of those without it. Of this group of 9 cases there was an elevated total protein in 6, although 2 (Cases 2 and 15) showed only a slight elevation. Repeat spinal-fluid examination in this group done within a few days after the original examination showed an increase in cells in 5 cases. All but 2 showed some abnormality in the cerebrospinal fluid after repeated examinations.

The pathologic process and distribution of the virus in the central nervous system in cases of poliomyelitis are more widespread than the amount of paralysis indicates. All parts of the central nervous system appear to be involved to some extent, but the changes indicative of injury or destruction of nerve cells are generally found in the motor nerve cells of the brain stem and spinal cord. The large, deeply staining anterior-horn cells of the cord seem to be most vulnerable ones.

In the case reported below, there was extensive sensory involvement, as well as motor involvement, and an almost complete transverse myelitis.

CASE 10. A 28-year-old soldier was well until 2 days before admission to the hospital, when he developed general malaise, felt feverish and had generalized muscular aches. The following day he developed dysphagia and noticed a change in the quality of his voice. Attempts to swallow even fluids were followed by regurgitation through the nose. Later on that day he noticed some weakness of the left arm.

Physical examination revealed stiffness of the neck and back, a positive Kernig's sign and weakness of abductor muscles of the left shoulder. There were no reflex or sensory changes. The temperature was 102°F., the pulse 100, and the respirations 22.

For the next 2 days the patient continued to run an elevated temperature with little change in the general picture. He was unable to swallow even liquids and was given 1000 cc. of pooled plasma, together with 5 per cent glucose and normal saline solution, up to 3500 cc. daily. On the 3rd hospital day he developed complete paralysis of both lower extremities. He was found to have paralysis of the bladder and of the rectal sphincter. There was loss of the abdominal and cremasteric reflexes. The deep reflexes of the lower extremities were absent. There was no plantar reflex on either side. Position sense in the lower extremities was completely lost. There was also diminished tactile sensation corresponding to the level of the 2nd lumbar segment. Pain and temperature sensations were unaffected. There was weakness of the abdominal muscles and the abductor muscles of the left shoulder. Closed drainage of the bladder was instituted.

The patient continued to run an elevated temperature for 6 more days. His condition remained much the same during that period, after which he began to show gradual improvement. On the 12th hospital day he was able to swallow liquids, then soft solid foods. On discharge to an Army medical center for poliomyelitis 6 weeks after admission, he still had paralysis of the bladder, but the tone of the rectal sphincter had improved. There was return in function of the abdominal muscles and many muscle groups of the lower extremities, although there was still fairly extensive involvement. The abductor muscles of the left shoulder were much the same as on admission.

A report from the medical center showed paralysis of the lower extremities involving a diffuse group of muscles. There had been moderate improvement, but there was still considerable involvement of the right gastrocnemius muscle. Bladder paralysis was still present, but function had recovered sufficiently so that the use of a catheter was no longer necessary. The rectal sphincter had returned almost to its normal tone. This report covered the status of the patient 7 months after the onset of his illness.

Approximately 50 per cent of the patients in this series received both pooled plasma and penicillin. Plasma was given in doses of 500 to 1500 cc. Penicillin was given intramuscularly, with an average total dosage of 1,680,000 units.

The evaluation of any therapeutic measure in anterior poliomyelitis is extremely difficult. In any such appraisal it must be borne in mind that a relation between the severity of the earlier symptoms and the ultimate appearance of the paralysis is inconstant: the death rate and the amount of residual paralysis vary greatly from place to place and in different epidemics. Furthermore, none of our patients were admitted in the preparalytic stage. So far as could be determined, neither plasma nor penicillin had any effect on the course of the disease. Convalescent poliomyelitis serum has been used in preparalytic states of poliomyelitis without benefit,[2] so that it is not surprising that no therapeutic results were obtained with pooled plasma given when paralysis or paresis had already set in. In addition, penicillin is reported to have no effect on the poliomyelitis virus.[3, 4]

The hot-pack treatment, as advocated by Sister Kenny, was carried out on all but 2 patients. The patients with involvement of the lower extremities were placed on a mattress stiffened by a board placed over the springs and so placed that there was a distance of several centimeters between it and the foot of the bed. The soles of the feet rested against the footboard, and the heels were in the space between it and the mattress. When muscle tenderness and pain cleared, physiotherapy, including baking, massage and passive and active motion, were instituted. There was little doubt that hot packs definitely diminished the muscle soreness and pain. No plaster casts or splints were used. The cases with involvement of the upper extremities showed only moderate or slight paralysis, and pillows were used for support.

For the patients unable to swallow, tube feeding was used, but in the first few days of the illness, when the temperature was elevated and the patient was acutely ill, this was not done, but instead fluids were given parenterally. It was believed that tube feeding during the acute phase caused a marked increase in pharyngeal secretions, requiring constant suction. In no case was tube feeding necessary for longer than two weeks. In 2 of the 3 fatal cases the Drinker respirator was used when the respiratory center became involved. It had no effect on the ultimate outcome, although life was prolonged for about twenty-four hours.

The patients could be followed only for seven weeks. Those who had residual paralysis were transferred to an Army and Navy general hospital for further treatment.

There were 3 deaths, all occurring in bulbar-involvement cases, and all from failure of the respiratory center. Thus, there was a 16 per cent mortality in the series as a whole and a 30 per cent mortality in the cases with bulbar involvement. The 7 pa-

tients with bulbar involvement who survived were able to swallow after a period of two weeks, but 5 of them had some residual. Two had slight dysphagia. Of these, one had a mild facial paralysis and the other a slight involvement of the sternomastoid muscle on one side. The 3 remaining patients had paralysis of the peripheral muscles. Of the 8 patients without bulbar involvement, 7 had some residual peripheral paralysis, although in each case improvement occurred. In 1 case there was complete recovery.

## Discussion

A short but violent outbreak of poliomyelitis occurring in adults has been presented. Poliomyelitis is primarily a disease of childhood. There has, however, been a gradual shift toward older age groups in poliomyelitis in both rural and urban populations in the last twenty years.[5]

This particular epidemic was characterized by a high incidence of bulbar-involvement cases. Stebbins et al.[6] reported on an outbreak of 20 cases, 13 of which were of the bulbar type; 12 of these terminated fatally. The incident of bulbar involvement varies with different epidemics. Lemmon,[7] in an analysis of 49 cases occurring in an epidemic in Pennsylvania, reports an incidence of bulbar involvement of 12 per cent. Fischer et al.[8] also report an incidence of 12 per cent, in a Toronto epidemic. Generally speaking, the incidence of bulbar involvement varies between 5 and 10 per cent.

The relation between tonsillectomy and bulbar poliomyelitis has been definitely established. None of the patients with bulbar involvement in this series had had a recent tonsillectomy and the proportion of those patients who had had tonsillectomy in the past was no greater than that of those without it.

Of considerable interest was the large proportion of patients with no increase in cells in the cerebrospinal fluid. On the initial examination 53 per cent of the spinal fluids showed normal cell counts. It had been noted that the usual findings in the cerebrospinal fluid in cases of anterior poliomyelitis are an increase in cell count and a slightly elevated protein during the first week, with a gradual decrease in cells to the third week and with a gradual increase in total protein.[9] Cases without an increase in the cell count, however, have been reported,[10–13] and the incidence of cases without cellular response in the spinal fluid has been estimated at 12 per cent.[11] In the Los Angeles epidemic of 1934, approximately 33 per cent of the patients had normal cell counts.[12] Similarly, Jensen[13] has reported 36 per cent of 3340 cases occurring in Denmark with normal cell counts.

Of particular interest is the case discussed above. The albuminocytologic disassociation is obvious. As is well known, this is a cardinal finding in the Guillain–Barré syndrome (infectious polyneuritis). It will also be noted that in Cases 3, 5 and 9 this disassociation was also present. Cases of infectious polyneuritis occurring during poliomyelitis epidemics have been reported.[14] An autopsy performed in Case 3, however, revealed the typical pathologic findings of poliomyelitis.

These observations demonstrate the difficulties encountered in the differential diagnosis of poliomyelitis and the Guillain–Barré syndrome. Different clinical criteria have been mentioned in numerous publications; they concern the mode of onset, the distribution of the paralyses and the laboratory findings. Progressive paralysis with diffuse symmetrical involvement, involvement of the facial nerve and albuminocytologic disassociation have been brought forth as differentiating the Guillain–Barré syndrome from poliomyelitis. The usually favorable outcome has also been pointed out as a differentiating point. Recent statistics, however, show the occurrence of a high mortality rate in polyneuritis.[15] On the other hand, complete recovery following an attack of poliomyelitis is frequently observed. It will be noted in the case reported above that many of the features of the Guillain-Barré syndrome were present. The course of the disease, however, was not that usually seen in this syndrome. Jervis et al.[16] reported a case in which the clinical manifestations and laboratory findings that are considered typical of the Guillain–Barré syndrome were seen and in which autopsy indicated acute poliomyelitis. They believe that differentiation based on clinical symptoms, observations of the spinal fluid and the final outcome is open to question and that this raises the problem whether the two diseases are distinct entities or different clinical manifestations of the same agent. The point can only be settled from an etiologic point of view by isolating the poliomyelitis virus or another virus from patients with infectious polyneuritis.

## Summary

The symptoms and physical and spinal-fluid findings in a short but explosive epidemic of anterior poliomyelitis are described.

An unusually high percentage of cases with bulbar involvement occurred.

A large percentage of the cases failed to show the cellular response usually seen in the spinal fluid in poliomyelitis.

The albuminocytologic disassociation described in the Guillain–Barré syndrome was found in 3 of the 18 cases in this series.

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# TETANUS, WITH DEATH DUE TO ASEPTIC DURAL SINUS THROMBOSIS

## Report of a Case

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THE following case of tetanus is reported because of several unusual features, one of which — aseptic dural sinus thrombosis — was apparently the cause of the fatal outcome.

### CASE REPORT

P. G., a 6-year-old boy, entered the Elliot Hospital on September 1, 1945, with the chief complaint of difficulty in swallowing of 1 week's duration. Three weeks prior to entry, a wood splinter penetrated deep into the left anterior tibial area. Part of the splinter was removed and the wound was dressed at home. The patient was well until 1 week prior to admission, when a "frozen" expression appeared on his face and he had slight difficulty in swallowing. Four days prior to entry, there were painful muscular contractions at night. On the day of admission difficulty in walking developed.

The family and past histories were noncontributory. The patient had had measles as an infant. He had had no inoculations or immunizations.

Physical examination disclosed a well developed, well nourished and fairly well hydrated boy, who was alert and co-operative but somewhat apprehensive. Skin turgor was good. The skin was tightly drawn over the contracted facial and abdominal muscles. All the muscles were hypertonic and resisted passive motion. The neck was slightly retracted and the back was slightly hyperextended. All deep tendon reflexes were hyperactive. Kernig and Brudzinski reflexes were markedly positive. There was severe pain on attempted flexion of the neck, which was extremely stiff. The Babinski reflex was negative. Trismus and risus sardonicus were present. The mouth could be opened to 1 cm. between the teeth anteriorly. There was a nearly healed, nontender stab wound 3 mm. in diameter on the left anterior tibial area.

The red-cell count was 4,960,000 and the white-cell count 13,800, with 81 per cent adult and 1 per cent young neutrophils, 16 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. The hemoglobin was 13.9 gm. Blood Hinton and Mazzini tests were negative. The patient was incontinent, and no urinalysis was done on admission. A lumbar puncture was done shortly after entry. The spinal-fluid sugar was 88 mg. per 100 cc., and the protein 18.7 mg. Pandy's reaction was negative, and the gold-sol curve was normal. Culture of the spinal fluid showed no growth.

The wound was excised and sodium perborate dressings were applied. Histologic examination of the excised area showed granulation tissue beneath an intact epidermis. Yellow foreign material, probably of vegetable origin and surrounded by large foreign-body giant cells and chronic inflammatory exudate cells, was seen. Gram stain showed large numbers of gram-positive bacilli, thought to be tetanus bacilli, and gram-positive cocci near the foreign bodies and in the adjacent soft tissue.

A diagnosis of tetanus was made, and treatment was begun shortly after entry. An initial dose of 40,000 units of tetanus antitoxin was given intramuscularly into the buttocks. Forty-five milligrams of Nembutal was given at entry and 33 mg. every 3 hours thereafter. Sodium luminal in doses of 65 mg. was given intramuscularly for acute spasm when needed. The patient was placed in a dark, quiet room. Hydration and dietary status were maintained by a special liquid formula taken through a straw. The formula was based on whole milk with added Dextrimaltose, sodium chloride, vitamin B complex and vitamins A, D and C. Other nourishing liquids and water were given by mouth as the patient tolerated them.

On the 2nd day, more frequent and severer painful muscular spasms of a generalized nature began, and the temperature rose to 101.8°F. Swallowing seemed easier. The abdominal and limb muscles were more spastic, and the neck and back more rigid. A dose of 10,000 units of tetanus antitoxin was given intramuscularly and repeated on the 3 following days. On the 3rd day, the patient rested and slept fairly comfortably. He was still incontinent of urine. Muscular rigidity continued to be marked. The rectal temperature varied from 99.8 to 101°F.

During the next 4 days, there was steady improvement. Trismus and muscle spasticity decreased, there were fewer severe muscular contractions, and the patient was able to speak and smile more normally. On the 7th day, however, the patient vomited a small amount of yellow-green material. The vomiting continued despite sedation and on the 8th day became projectile. All oral medications were vomited, and the patient became extremely restless. The temperature had risen to 104.6°F., the pulse to 136, and the respirations to 36. One thousand cubic centimeters of normal saline solution was given by clysis. Later in the day the rectal temperature rose to 106.6°F. Penicillin in doses of 10,000 units every 3 hours was given intramuscularly.

On the 9th day, a surgical consultant examined the patient because of abdominal pain and moderate distention, but believed that there was no intra-abdominal disease. Later in the day the temperature dropped to 102.6°F. The pulse was 128, and the respirations 30. Projectile vomiting continued and became more violent. The red-cell count was 6,380,000 and the white-cell count 15,400, with a moderate shift to the left in neutrophils — probable evidence of hemoconcentration and dehydration, a factor to be considered in the light of vomiting and perspiration. The hemoglobin was 15.3 gm.

On the 10th day, oxygen was started. Blood examination showed correction of the hemoconcentration. The red-cell count was 4,760,000. Urinalysis showed many hyaline and granular casts but was otherwise negative. A second lumbar puncture was performed. The dynamics of the spinal fluid could not be ascertained because of difficulty in controlling the patient. The fluid contained 26 red cells and 1 lymphocyte per cubic millimeter. Pandy's reaction was negative. No organisms were seen in the smear of the fluid. The protein was 25 mg. per 100 cc. Culture showed no growth.

Projectile vomiting continued, and terminally the vomitus contained a large amount of greenish-black material of foul

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odor, which was partly aspirated into the lungs. Artificial respiration and dependent drainage were of no avail, and the patient expired.

*Autopsy* (performed by Dr. S. M. Brooks). The body was that of a moderately emaciated child. There was a healing scar at the site of the excision of the original infection. The bronchi contained green-brown gastric material, and there were a few areas of red-brown mottling on the cut surfaces of the lungs. The stomach was somewhat dilated and contained thick, greenish-brown fluid. The urinary bladder was empty.

The dura of the brain was of normal thickness and appearance and was not adherent to the calvarium. The right lateral sinus contained an ante-mortem thrombus extending into the superior sagittal sinus and the jugular vein. The thrombus was not adherent to the walls of the sinus, and the intimal lining of the sinus appeared smooth and glistening. The cerebral vessels were not remarkable. The convolutions of the brain were slightly flattened, and there was slight narrowing of the sulci. The brain weighed 1360 gm. — approximately 10 per cent more than normal for this age. Coronal sections showed a slight pink tinge in some places in the white matter, and the nuclei of the brain stem and medulla were pinker than normal. The petrous and mastoid bones and accessory nasal sinuses were not remarkable. The spinal cord did not appear grossly abnormal except for a slight pinkness of the cut surfaces of the anterior horns in the cervical and lumbar enlargements. A blood culture showed no growth in 9 days. Other tissues and organs showed no lesions.

Microscopical examination of the thrombi from the dural sinuses revealed a few organizing fibroblasts. The dura was not inflamed, and the thrombi were not adherent. The pulmonary alveoli contained gastric contents, and there were small hemorrhagic areas throughout the lungs. The basal ganglions and midbrain nuclei showed dilated blood vessels. The excised wound showed new fibrous tissue deep in the wound and close to a nerve bundle, but there was no foreign material or foreign-body giant cells about the wound. Other tissues showed no histologic lesions.

According to Pratt's[1] method of rating, this case may be considered one of moderately severe tetanus infection. In retrospect it is thought that closer attention should have been paid to hydration and dietary status, in view of the extremely warm weather and the patient's perspiration. The dural sinus thrombosis may well have been the result of dehydration, as shown by Bailey and Hass.[2] It might have been well to have given half the initial dose of 40,000 units of antitoxin intravenously to fix rapidly any circulating toxin, but the total dose was adequate according to Pratt,[1] although inadequate according to Vinnard.[3] Penicillin might have been given earlier and in greater doses with good effect.[4, 5]

This case demonstrates the advisability of active immunization against tetanus infection early in childhood. It also shows the necessity for early and complete débridement of wounds likely to harbor tetanus bacilli and the wisdom of administering antitoxin in adequate amounts soon after injury in nonimmunized persons.

The unique feature of this case, the aseptic dural sinus thrombosis, appears to have been the direct cause of death. According to Bailey and Hass,[2] few patients survive this condition, and autopsy of survivors shows severe brain damage. In 52 per cent of the 80 cases reported by these authors, the dural sinus thrombi were septic. All the patients with nonseptic dural sinus thrombi were less than thirty months old, and the average age was nine months. As a rule a period of extreme hyperthermia precedes death. The patient in the case reported herein was six years old and had a rectal temperature of 106.6°F. three days before death.

Neurologic signs in these cases are diverse and undependable. The spinal fluid may or may not be under increased pressure; it is usually xanthochromic and contains 10 to 1000 red cells per cubic millimeter. Tests for increased globulin are generally positive; the sugar level is normal.

The terminal findings in this case may be correlated with the dural sinus thrombosis, which probably began to form on the seventh hospital day.

## Summary

A case of tetanus in which death was probably due to an aseptic dural sinus thrombosis is reported, and certain of the unusual findings are discussed.

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# MEDICAL PROGRESS

## PULMONARY TUBERCULOSIS

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ALTHOUGH a voluminous literature covering the field of pulmonary tuberculosis has appeared during the last year, few outstanding advances have been made. Many papers, however, deserve mention because of their help in the diagnosis and treatment of the disease.

### Control and Case Finding

In the last few years, since the advent of the miniature roentgenogram, case finding has achieved an unprecedented popularity. Fortified by public funds, the United States Public Health Service and other agencies are now well in the midst of programs to search for tuberculosis in every nook and cranny in this country. As a result, the number of known cases of tuberculosis has increased, but facilities for their care in sanatoriums have not expanded at a comparable rate. This lag in accommodations is noted and lamented in many recent publications.

Hilleboe[1] estimates that at the end of 1945 about 20,000,000 persons in the United States aged twenty years or older (1 in every 5 adults) had chest roentgenograms taken by the armed forces, health departments, industrial firms or voluntary agencies. But case finding is only one step in the control of tuberculosis; isolation and treatment are equally important. Patients with cases of active tuberculosis must be given medical care and must be isolated to prevent further spread of the disease. Hilleboe points out that there is a lack of vision in case finding if treatment is delayed by a shortage of sanatorium beds, adding: "In every industrial community in which a tuberculosis control campaign is undertaken, plans must be made for the provision of a sufficient number of beds. Temporary facilities may, for a time, be utilized until the people, realizing the seriousness of the community's plight, will demand the construction and maintenance of the necessary hospitals."

Elsewhere, Hilleboe and Gillespie[2] phrase this same thought somewhat differently:

> Unfortunately, after a physician has made a diagnosis of active pulmonary tuberculosis and has recommended sanatorium care, it may be found that sanatorium beds are not available. Therefore, it is necessary for physicians to care for these patients at home. This means that the physician must employ techniques used in the modern sanatorium including bed rest, nursing care, isolation, precautions, and general and personal hygiene.

If a physician keeps a patient close to the sanatorium routine at home while awaiting admission to a sanatorium, he is frequently surprised, at least in my experience, at the progress the patient exhibits in a short time.

The trend of the times in case finding is further illustrated by statistics from the State of New York, where Mikol and Plunkett[3] report that from 1924 through 1939 in men, and from 1924 to 1941 in women, there was an almost steady decline in the annual number of cases of respiratory tuberculosis. Among the former a striking reversal of this trend began in 1940, reaching a peak in 1942, during which the number of cases was 38 per cent higher than in 1941. This increase was largely due to an increase in the minimal cases in the age group from twenty to thirty-four years. Mikol and Plunkett believe that this increase is due to the discovery of more cases by the various mass surveys rather than to any actual increase in the development of new cases. The greater incidence of pulmonary tuberculosis in young men and women is probably more apparent than real.

The extent to which case finding and hospitalization of discovered cases will eventually lower the tuberculosis death rate is not known. Nor are there reliable data regarding the number of early cases that will reactivate in spite of prompt hospitalization. Nevertheless, the tuberculosis mortality rate continues to show a gratifying decline. In the United States in 1944 it was at its lowest figure: 41.3 per 100,000 population, as compared with 42.6 in 1943 and 43.1 in 1942. In Massachusetts, the death rate in 1944 was 40.8, as compared with 42.7 in 1943. According to preliminary estimates for 1945, the number of deaths from tuberculosis has continued to decline, but no exact figures are available. It must be pointed out, however, that statistics collected during the war years are not wholly reliable because of both the large shift of population groups and the considerable number of the population that has been overseas.[4]

### *Tuberculosis in Persons over Fifty*

Myers[5] points out that tuberculosis mortality is higher among Americans after the age of fifty years than at any other time in life, and that this fact is apparently not generally recognized, as indicated by the belief that human beings rarely have tuberculosis in the later decades of life. Since the average

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age of the population is increasing, the number of cases of tuberculosis in the aged is showing a commensurate rise. Besides, the disease in the elderly may be even more prevalent than mortality statistics suggest, since a significant number of deaths are not accurately reported. Myers cites the case of a man who had had a cough and a positive sputum for thirty years and who had presumably infected two daughters. At the age of eighty-two this man spent the winter in another state, where he became acutely ill and died within twenty-four hours. The local physician had no opportunity to examine him adequately. On the death certificate the cause of death was stated as "coronary disease," and no mention was made of tuberculosis.

Although tuberculosis is frequently discovered in elderly persons, Myers cautions that the diagnosis should not be made without adequate evidence. An aged person with a chronic cough and expectoration does not necessarily have pulmonary tuberculosis. Symptoms, signs and x-ray appearance are not pathognomonic. The only absolute diagnostic finding is the presence of tubercle bacilli, confirmed by culture or animal inoculation.

*Tuberculosis among Nurses*

On the basis of considerable evidence obtained from reviewing the medical literature and from his own experience, Cameron[6] believes that nurses are exposed to a real hazard while caring for tuberculous patients. He emphasizes that nothing is gained by minimizing the facilities for tuberculous infection that exist in a sanatorium. Reported statistics indicate that the incidence of tuberculosis among nurses varies from 1.6 to 6 per cent, with a probable average of about 3 per cent. Yet, surprisingly, practically all superintendents of sanatoriums agree that tuberculous disease among their staffs is rare. The reason for this apparent contradiction, Cameron points out, lies in the fact that there is no follow-up of those employees who have left the institutions. Another possible reason is that many nurses are covered by the blanket classification "housewife" in hospital statistics and reports. Actually there are many registered nurses, attendant nurses and various ward helpers whose occupation at the time of admission to the sanatorium is "housewife" and whose earlier employment and possible infection are ignored.

Statistics regarding tuberculosis among nurses are probably much too low. Cameron observes that the repeated infections to which nurses are exposed are an undoubted risk. The greatest danger, of course, lies in young girls whose reactions to the Mantoux test are originally negative, although there is theoretical danger even to those whose reactions are positive. Cameron carries this thesis still farther, pointing out that to control tuberculosis among nurses working in sanatoriums the administrators should concern themselves with the mental and spiritual well-being, as well as the physical status, of the employees. He writes as follows:

> An emancipated spirit fortifies a well-tended body, and strength of body and serenity of mind are the best defences against tuberculous invasion. . . . The living and working conditions of tuberculosis nursing must be good. Mental freedom is just as important as physical well-being.

It is my belief that if more sanatorium administrators placed greater value on the wisdom of these words, there would be far less of a nursing shortage in many institutions.

*Tuberculosis in Repatriated Prisoners*

Brooke[7] provides a partial answer to the question of the extent of tuberculous involvement in repatriated prisoners of war. Of course, his figures are not wholly adequate in that they do not include patients who died in prison camps because of the disease. Of 1507 prisoners repatriated from Japanese camps he found that 118 (7.8 per cent) had active or questionably active pleural or pulmonary disease. Of these, 24 were believed to be questionably minimal, and 33 minimally active. Repatriated prisoners had a lower incidence than had been anticipated.

*Tuberculous Families and Household Associates*

Many workers have speculated on the factors that control the incidence of clinical tuberculosis in a given household. It is a frequent clinical experience that not every person in a household develops active tuberculosis even when the extent of the exposure to an open case is roughly comparable in all the members of the household unit. To determine the reasons for this variability, Puffer and her associates[8] investigated family contacts in Williamson County, Tennessee. Careful studies of the associates of 519 white and 111 colored index cases revealed that the prevalence among white associates increased from a low rate in persons under fifteen years of age to a high rate for those thirty-five years and over. The incidence among colored associates did not show this distribution: relatively high rates were found in all age groups. In white associates thirty-five years of age or older 12.9 per cent of the blood relations had manifest tuberculosis, whereas only 7.4 per cent of those not related had the disease. In the age group fifteen to thirty-four years the attack rate for white household associates related by blood was 0.8 per cent, and for those not related it was 0.3 per cent. Obviously, blood relatives show a greater attack rate and a greater prevalence rate than those not related.

These data are supplemented by the report of Telford and Garten-White,[9] of the Los Angeles County Health Department. Whereas they had been inclined to discount the lay conception that there is a familial susceptibility or resistance to the disease,

they are forced to conclude that there may be some factual or at least statistical basis for this relief. Their figures showed that a comparatively small proportion of the families exposed presented nearly all the new cases, and they believe that the attributes that make these families more than ordinarily susceptible deserve earnest study. If the characteristics of these groups can be recognized, public-health efforts can be devoted more intensively to such families than to the community at large.

It is pointed out that a crowded living condition, although a major contribution to a greater familial incidence of tuberculosis, is not the only factor involved. A survey of patients in 1940, for example, revealed that about 5.0 per cent of 1637 contacts developed active reinfection tuberculosis six months or more after the discovery of the first known case in each of the families. In 1944, in spite of apparently improved social and economic conditions, the attack rate was found to be insignificantly lower — 4.8 per cent. Other surveys conducted at the same time in congested areas yielded an attack rate of only 0.5 per cent. The great hazard in families with a high attack rate is apparently due not only to the direct spread of the infection but also to other factors and conditions favoring the spread. Telford and Garten-White therefore believe that some inherent fault in either physical or mental make-up makes the members of such families more susceptible than the average person, or that contributory domestic habits have not been overcome by the usual public-health education and supervision. They write as follows: "Isolation of active cases of tuberculosis, either outside the home or in the home with intensive supervision, should be stressed in proportion to the number of cases in the family or to cases known in the recent family history."

On the basis of these detailed investigations one can reasonably conclude that it takes more than mere contact with the tubercle bacillus to develop clinical disease. The factor of familial susceptibility must be considered in the management and prognosis in any given case. Further elucidation of the factors of familial susceptibility is certainly indicated.

## Anatomical Considerations

Since bronchoscopy and surgery are playing such an important role in the diagnosis and treatment of pulmonary disorders, a wider understanding of the segmental anatomy of the tracheobronchial tree is essential. Localization of a pulmonary lesion in relation to its appropriate bronchopulmonary segment often helps clarify the nature of a suspicious roentgenologic shadow, and may provide a clue to its proper management. No longer can it be considered adequate to describe a "spot" as being at "the level of the third anterior interspace." In the following three studies[10–12] one can obtain the essentials for a more complete understanding of the tracheobronchial tree and its pulmonary segments as viewed by the anatomist, the bronchoscopist and the roentgenologist.

The anatomist's point of view is presented by Boyd[10] in a series of excellent dissections and exquisite colored plates. Briefly, some of the significant facts are as follows:

> *Right bronchial tree.* The upper or *superior-lobe bronchus*, which arises almost at the bifurcation of the trachea, is very short, branching almost immediately into three stems — the apical, anterior and posterior segmental branches. The apical segmental branch divides into anterior and posterior rami. The anterior one divides into a lateral ramus going to the axilla and an anterior ramus descending to the inferior portion of the upper lobe. The posterior segmental branch divides into a posterior ramus, with its posteriorly placed orifice and its predilection to abscess, and a lateral ramus. The *middle-lobe bronchus* divides into a medial and a lateral segmental bronchus, which show considerable anatomic variation, and there is some shifting from one segment to another. For this reason resection of either the medial or lateral segment is technically difficult, and if operation is indicated both segments are usually resected together. The *lower-lobe bronchus* divides first into a superior segmental bronchus, which has a posterior horizontal distribution and, surgically, can be readily identified and removed separately. Between the superior bronchus and the remaining segmental bronchi of the right lower lobe there is an interval of 1.5 cm., which is the common stem of the four segmental bronchi that reach to the base or the diaphragmatic surface of the lung.
>
> *Left bronchial tree.* The upper or *superior-lobe bronchus*, which originates farther down on the left side than on the right, arises from the anterolateral instead of the posterolateral surface of the main bronchus. It divides into a superior and a lower (or lingular) division. The upper division gives off an apical posterior segment and an anterior (or pectoral) segment. The lower or lingular division has superior and inferior segments, the lingula being analogous to the middle lobe on the right. The inferior or *lower-lobe bronchus* gives off several segmental branches that are designated as superior, anteromedial basal, lateral basal, and posterior basal. As on the right, the superior segment has its orifice posteriorly, close to the point of origin of the bronchus itself. The basal segments on the left differ from those on the right in that they are three in number instead of four and usually branch by trifurcation rather than by bifurcation.

Hagens[11] dissected the lungs of 20 cadavers to clarify the appearance of the bronchial tree from the standpoint of the bronchoscopist. He was thus able to map out the various orifices that are such important landmarks, to determine their diameters and to make many measurements to establish their usual relations. This paper should be read in conjunction with that of Boyd,[10] since the data and descriptions tend to supplement each other.

Clarification of the anatomic arrangement of the tracheobronchial tree makes more readily understandable the valuable series of articles by Robbins and his associates[12, 13] on the roentgenologic appearance of the segmental collapse of the lung. These investigators recommend that when pulmonary disease is suspected the patient be studied fluoroscopically and that in addition he have a routine posteroanterior film, a lateral film and an anteroposterior Bucky or Swedish-grid roentgenogram. With these few studies approximately 80 per cent of patients with pulmonary disease need no further roentgenologic investigation to establish the diagnosis. The usual diagnostic criteria of segmental

collapse of the lung, Robbins et al. point out, are an abnormal shadow of increased density, elevation of the diaphragm, displacement or shift of the mediastinum and narrowing of the rib spaces. After a detailed analysis of 1200 cases of tumor, bronchiectasis, foreign body and tuberculosis, they were able to add three more criteria to this original list: the appearance and position of the hilar shadows, the arrangement of the vascular shadows and the demonstration of the actual size of a lobe as determined by the appearance and position of the septums or fissures of the lung. Displacement of a hilus upward, for example, indicates possible collapse of an upper lobe.

Although collapse of an entire lung or a major portion thereof is usually readily recognizable from established criteria, segmental collapse may be more difficult to identify. Collapse of a lower lobe occurs rather frequently but is often overlooked or misinterpreted because the shadow of increased density is small and so located that it is hidden by overlying structures, such as the spine, diaphragm and mediastinum. Usually the first sign of collapse of a lower lobe is a posterior displacement of the interlobar septum. Lung markings of the collapsed lobe later become crowded together. If the collapse is confined to the dorsal division of the lower lobe it may be identified as a triangular area of density and by the sharp angulation of the posterior portion of the major interlobar septum. Since bronchiectasis usually spares the dorsal division, whereas tuberculosis and lung abscess are often found in that area, accurate localization of the collapse is frequently an aid in differential diagnosis.

Collapse of the right middle lobe of the lung also occurs frequently but is often confused with interlobar effusion. Complete obstruction of the bronchus to the right middle lobe causes the lobe to decrease in size and assume a pyramidal shape, with the base against the right border of the heart and the apex extending toward the lateral chest wall. The result is a loss of definition of the right border of the heart. In this event the lateral view is the most important single factor in the examination, and its appearance may be deceptively like that of a pleural effusion. A lordotic view may help further in the differentiation of these two conditions.

Collapse of a single lobe of a lung is most frequently misinterpreted in one of the upper lobes, where it is confused with a localized area of consolidation, a mediastinal tumor or an aortic aneurysm. In some cases it may be completely overlooked. One of the first signs of collapse of an upper lobe is displacement of the major septum anteriorly and superiorly as determined in the lateral film. Careful attention to detail on all the x-ray films is essential to accurate diagnosis of collapse and to differentiation from other pathologic conditions.

An understanding of the bronchial pattern also helps in an evaluation of the status of a bronchus that drains a tuberculous cavity. According to Camiel,[14] the roentgenologic appearance of the lung in the area between a tuberculous cavity (or the site of a previous cavity) and the hilus is of special importance. This portion of the lung contains the regional bronchi and the peribronchial vascular and lymphatic channels that drain the area of the parenchymal lesion toward the lung root. These draining bronchi, which are frequently involved in the tuberculous process, can often be visualized roentgenologically, and their appearance depends on the severity and duration of the underlying process or disease. Bronchial thickening due to edema or thickening resulting from extension of the disease into the bronchus with subsequent fibrosis increases the visibility of the bronchial shadow and thus makes possible a diagnosis of endobronchial tuberculosis.

### Bronchospirometry

With the greater interest in the detailed anatomy of the bronchial tree during the last few years there has been a corresponding interest in greater refinements of technic for determining the functional capacity of the lungs. In many cases it is no longer adequate to make one determination of a patient's vital capacity in the belief that it provides a reliable gauge of his pulmonary function. The vital capacity can be considered rather as a rough guide that fails to disclose any information concerning the function of each lung and therefore may be misleading.

Bronchospirometry, on the other hand, provides the additional data that are often lacking. With this procedure it is possible to make many different determinations on each lung (such as tidal air, respiratory rate and vital capacity) and to decide what functional share each lung is contributing to the total. Some of the significant facts that can be learned from bronchospirometric studies have been recently reviewed by Pinner, Leiner and Zavod,[15] who found that bronchospirometry often revealed decreased function in one lung when regular spirometric studies were normal or nearly normal. For example, they cite the case of a twenty-nine-year-old man with right pneumothorax, whose vital capacity on spirometry was 2650 cc. Maximum breathing capacity divided by minute volume was 11.3, a finding consistent with a normal respiratory reserve. Yet on bronchospirometry the oxygen intake of the right lung was discovered to be only about a third of the total oxygen intake: in spite of a normal respiratory reserve, the right lung contributed only about 30 per cent of the total oxygen intake instead of its normal contribution of 54 per cent.

One of the most valuable findings resulting from these bronchospirometric investigations is the demonstration that a marked discrepancy may exist between the clinical findings, the x-ray appearance and the actual function of the lung. Cases are cited

to show that a slight amount of fibrosis (as determined by x-ray study) may be accompanied by a considerable amount of functional damage. Conversely, in a lung that appears on x-ray examination to be heavily infiltrated or even riddled by cavities, the impairment in function is hardly appreciable. Curiously enough, when special studies were made on patients whose lung function was extremely poor, it was found that practically all these patients had either obliterative pleuritis or phrenic paralysis. Pinner et al. emphasize the fact that pleural involvement that cannot always be diagnosed by roentgenologic examination may lead to severer functional damage than a more obvious parenchymal lesion.

Collapse therapy (pneumothorax) causes a reduction in the oxygen intake of the collapsed lung. Compensation for this decrease is accomplished by both a commensurate increase in the contralateral lung and a cardiovascular factor. The respiratory burden on the contralateral lung is considerably less than one might anticipate. It therefore follows that if a patient with unilateral pneumothorax is dyspneic at rest, the cause is not likely to be found in the extent of his collapse but rather in a possible functional impairment of the contralateral lung. That therapeutic pneumothorax (or the disease itself) may leave the lung with permanent functional disability is demonstrated by the fact that re-expanded lungs show some degree of respiratory impairment. Twenty-six cases of thoracoplasty studied showed surprisingly less diminution in pulmonary function than those treated by pneumothorax. But, as Pinner and his colleagues[15] point out, more cases will have to be explored by this method before it can be certain that the differences detected are not merely the results of random sampling. An interesting side light brought out by bronchospirometric investigation is that immobilization by sandbags or by strapping with adhesive does not achieve a reduction in the ventilation or the respiratory work of the underlying lung.

Tests of pulmonary function, in a way, are analogous to those of renal function. In diffuse bilateral disease, the total function (as determined by routine spirometry) may provide all the data that the clinician needs. On the other hand, in unilateral disease or in predominantly unilateral disease or when surgery is contemplated, data regarding the function of each lung separately may provide invaluable information.

## Bed Rest

The recent discussions covering strict bed rest as a method of treatment have stimulated renewed interest in this type of therapy for tuberculosis. Obviously, strict bed rest is not without its limitations and contraindications in tuberculosis as in many other ailments. Peck[16] described the progress of a group of patients at the Detroit Municipal Tuberculosis Sanatorium who were placed on a regime of bed rest with instructions never to sit up, never to raise the head from the pillow and to lie as inertly as possible. Difficulties soon began to appear. Cough frequently increased, with roentgenologic evidence indicating poor drainage of secretions, and a few patients showed serious extension of the disease. Many complained of increased nervousness and fatigue. Peck concluded that strict bed rest may at times be harmful and may actually defeat the purpose for which it is given.

It was recognized soon after this experiment that rest in the supine position violated a well established surgical tenet — that drainage from abscess cavities must be free and adequate. Since most tuberculous cavities are posteriorly placed, such a position interferes with drainage, makes the cavity dependent, encourages toxicity and enhances spread. Because of these considerations, the regime at the Detroit Municipal Sanatorium was modified to allow the patient reasonable motion in bed, adequate drainage of cavities, relief from bronchial spasm and liquefaction of sputum by means of steam inhalations. The problems of muscular relaxation and mental repose — a much neglected aspect of treatment in the routine management of sanatorium cases — were also given consideration.

This new regime of treatment was then applied to 69 patients, most of whom had extensive bilateral disease and cavitation. Of these, 19 had cavity closure with conversion of sputum, 14 responded favorably enough to permit thoracoplasty, 26 were studied for an insufficient length of time, and 10 died. In a control group of cases (the difficulties in finding true controls are admitted), selected because of similar age and comparable lesions by roentgenogram, only 2 patients had cavity closure and sputum conversion, 7 progressed to thoracoplasty, 12 were discharged improved, and 48 died. In Peck's opinion carefully supervised bed rest is effective therapy, giving results entirely commensurate with the time and energy involved.

Elsewhere, Peck and Willis[17] direct criticism to so-called "postural rest," in which patients with unilateral cavitation are encouraged to lie on the cavity side with the idea that the uninvolved lung will be protected from positive sputum. They believe, with good reason, that such an argument is fallacious and that postural rest cannot maintain unilateral sepsis. They cite the case of a thirteen-year-old girl who had been kept on one side for three months, with consequent bathing and saturation of the dependent lung in its own secretions. Examination showed that this girl had extensive bronchiectasis of the upper lobe of the dependent lung, which may well have developed as a direct result of improper bed rest. No physician would give the same dose of insulin to all his diabetic patients, and yet the same dose and same type of bed rest is prescribed for all tuberculous patients in some sanatoriums.

This condemnation of strict bed rest for all patients is carried still farther by Bray,[18] of the New York State Hospital for Incipient Tuberculosis, who points out that few published reports substantiate the alleged value of strict bed rest for tuberculous patients who are in a good nutritive condition and entirely or practically free from symptoms. Contrary to some expressed opinions, early tuberculous lesions, especially those in the upper part of the lung, have a marked tendency to heal and are usually not progressive. This point is readily demonstrated in Bray's studies of 67 cases, whose lesions were less than a year old as determined by serial roentgenograms. In no case did the patient receive strict bed rest; all were ambulant from the time the disease was discovered, throughout their sanatorium stay and subsequently, for a period averaging thirty months. The results were favorable in 57 (85 per cent of these cases). Although the number of cases was too small for definite conclusions, this experience is comparable to the best statistics obtained with strict bed rest. Bed rest, like any other form of therapy, should be individualized both in the early and in advanced cases.

An ingenious but still unproved theory advanced by Dock[19] to account for the apical localization of pulmonary tuberculosis has some bearing on bed rest. Dock points out that in man the mean pulmonic arterial pressure is equivalent to 15 to 18 mm. of mercury, which, in turn, is equivalent to a column of blood 12 to 23 cm. in height. Since the apex of the lung is 15 to 30 cm. cephalad to the right ventricle, the pulmonic arterial pressure in the upper 5 cm. of the lung, even in systole, is at most equivalent to 10 mm. of mercury. Because a pressure equivalent to about 15 mm. of mercury is required to overcome the difference in colloidal osmotic pressure between the plasma and the pulmonary tissue fluid, it is likely that no lymph is produced in most adults while they are in the erect posture. As a result, it is claimed, few lymph-borne and cellular antibodies reach the apical portions of the lung while a person is sitting or standing.

But Dock affirms that this fact does not mean that a person with tuberculosis must lie flat on his back all the time; it simply means that if he is taking bed-rest treatment he should be recumbent and not sitting up. At least part of the day should be devoted to recumbency to overcome the hydrostatic pressure within the pulmonary circuit. Dock's conclusion is as follows:

> It is quite possible that if the patient were allowed up, when he felt strong enough, for ten to thirty minutes four or five times a day, his moral and physical strength would be better preserved or more quickly restored. Even if this were permitted in the mornings, when the afternoon temperatures were elevated, it might do more good than harm.

Such a program might enable a patient to accept recumbency as a therapeutic measure with a greater degree of physical and mental ease and might thus make the entire treatment more effective.

### Pleurisy with Effusion

It is becoming increasingly evident that pleurisy with effusion, especially in young adults, most frequently has a tuberculous etiology. Farber's[20] recent follow-up studies clearly demonstrated that a significant number of patients with pleural effusion develop pulmonary tuberculosis. Of 111 patients followed for three years or longer, 38 (34 per cent) developed parenchymal disease, and 27 died. This indicates that the prognosis in cases of pleurisy with effusion should be guarded.

More recent investigations are consistent with this point of view. For example, Bird's[21] evaluation of the clinical course of 7 cases of alternating pleurisy with effusion in patients between the ages of twenty-one and thirty-six, with an average age of thirty-two, demonstrated a tuberculous background in all but 1. In several cases, tubercle bacilli were found on culture or guinea-pig inoculation when direct smears were reported as being negative. It must be stressed that the more delicate the test, the greater the likelihood of recovering the tubercle bacillus. Close[22] also found that as the bacteriologic technic improved, the number of proved positive cases increased from an average of 40 per cent to one of 70 per cent. In his most recent series of cases, among 159 young adults hospitalized for pleural effusion he recovered tubercle bacilli by culture on the Lowenstein–Jensen medium in 90 per cent of the cases in which the diagnosis of tuberculosis was eventually made on clinical grounds. He states: "No opportunity for culturing should be neglected. Even 1–2 cc. of what looks like blood from an unsuccessful attempt at aspiration should be put on culture medium. From three such lung punctures tubercle bacilli have been obtained."

Similarly, Feldman and Lewis[23] are of the opinion that bacteriologically sterile effusions carry the same import as those that are positive, active caseous tuberculosis being directly responsible for the onset of the effusion even when the fluid remains sterile. At the Rhoads General Hospital they thoroughly investigated 59 patients with pleural effusion, especially for the presence of tuberculosis. The fluid was on the right side in 39 cases, on the left in 18 and bilateral in 2. The onset of the disease was described as "insidious" in 34 cases, "acute following a prodrome" in 18, and "acute, fulminating" in 9. In 2 cases with insidious onset, the patient developed a fresh pleural effusion on the opposite side after the original one had subsided; both cases had suggestive parenchymal infiltration and hilar enlargement. Feldman and Lewis conclude that pleural effusion occurring in young persons in whom no other readily demonstrable cause exists can be considered tuberculous until clearly proved otherwise.

Since tuberculosis figures so significantly in the etiology of pleurisy with effusion it is essential that these patients be followed, like any tuberculous person, by frequent check-up and x-ray examinations. Feldman and Lewis recommend such a follow-up to extend for five years after the onset of the effusion, with special emphasis on the first year. For therapy, they advise complete evacuation of the chest (in stages, if necessary) and the introduction of 200 to 300 cc. of air into the pleural cavity to obtain better x-ray visualization of the lung parenchyma. It seems logical that if tuberculosis is suspected, the contacts of all patients with pleurisy and effusion should be investigated to determine the possible source of the infection.

## Chemotherapy and Antibiotics

### *Streptomycin*

Each year some new therapeutic weapon seems to offer the victims of tuberculosis a quick and dramatic rescue from their long and costly illness. This year the "hope on the horizon" is streptomycin. Although its precise indications and limitations have not been worked out in human tuberculosis, there can be no question about its effectiveness in animals. Injected into guinea pigs, streptomycin was found to exert a striking inhibitory action on the activities of *Mycobacterium tuberculosis* in vivo but did not succeed in eliminating or killing all the bacilli in the animals.[24] In mice, whose resistance to tuberculosis is greater than that of guinea pigs, a comparable effect was noted, and the suppressive action was characterized as marked even though the tuberculous infection was not completely suppressed.[25] After a more extensive and better controlled series of experiments, Hinshaw and Feldman[25] reported that streptomycin appeared to be more effective than any of the sulfonamide drugs and much less toxic for guinea pigs.

Under the direction of Hinshaw and Feldman[26] streptomycin therapy for human tuberculosis was begun in December, 1944. At first, small ineffective doses were used, with inconclusive results. With further knowledge of the pharmacologic properties of the drug, it was soon established that the minimal daily dosage should be 800,000 "S" units (1000 "S" units equal 1 mg. of streptomycin), and usually the patients received from 1,000,000 to 2,000,000 units by intramuscular injection at three-hour intervals. No serious toxic effects were noted, but in 4 cases sensitization to the drug was apparent, so that violent febrile reactions developed when the drug was administered after an interval of a few weeks. In some cases transient deafness and disturbance of vestibular function were observed, but it is not known whether this was due to the streptomycin or to some impurity. At any rate, of the 16 patients treated for one to three months, no rapid curative action was seen. Lesions that were soft and of known recent origin tended to improve promptly, but in some cases there was reactivation when the drug was discontinued. All that could be said for streptomycin was that it had a limited suppressive effect.

Subsequently, in a more detailed report, Hinshaw and Feldman[27] cited their experience with 54 patients with tuberculosis who had received streptomycin treatment for periods of more than four weeks. In each case the disease had shown a tendency toward unfavorable progression prior to the institution of therapy. In 21 cases the patients had pulmonary tuberculosis, which in 16 was far advanced with the addition of infiltrations of recent origin. Of the 21 pulmonary cases studied, objective evidence of improvement was observed in 16. An antibacterial action was not noted, but a suppressive effect was found so long as administration of the drug was continued. Streptomycin was also used in cases in which there were tuberculous sinuses, but in 3 of 5 cases the sinuses recurred after the drug was discontinued. In tuberculous empyema and in urogenital tuberculosis the results must still be regarded as inconclusive.

Supplementing this report by Hinshaw and Feldman, Cooke and his colleagues,[28] at the Yale University School of Medicine, recorded the recovery of a child with tuberculous meningitis. The infant was admitted to the New Haven Hospital on May 12, 1945, with convulsions, and the diagnosis of tuberculous meningitis was incontrovertibly established. Streptomycin was begun seven days later and continued for thirty days. Therapy was discontinued because of lack of the drug, but was resumed on July 9 for an additional twenty-nine days. At the time the report was written (December 31, 1945) the child was still alive and apparently improving, although there were some residual neurologic impairment, cervical adenopathy and abnormal pulmonary findings. Acid-fast bacilli had not reappeared in the spinal fluid, however.

### *Other Antibiotics*

The *Bacillus subtilis* produces a substance called "subtilin" that has a bacteriostatic action in vitro against the tubercle bacillus in high dilution (1:100,000) and appears to be germicidal in greater concentration (1:50,000).[29]

Mattick and Hirsch[30] isolated a streptococcus that destroys tubercle bacilli in vitro. On exploring the widely held notion that the acid in sour milk had a destructive action on tubercle bacilli, they found that it was not the acid per se or the lactic streptococcus that was responsible for the tuberculocidal action of sour milk, but another streptococcus — "the inhibitory streptococcus." This organism, they claim, produces sufficient antibiotic substance to kill or render avirulent up to 2000 tubercle bacilli per cubic centimeter of milk. These tests, which are preliminary, await confirmation.

*Chemicals*

Clinical interest in the sulfonamides is waning — perhaps rightly so. Their value in clinical tuberculosis is less than the earlier results seemed to indicate. For example, at the Firland Sanatorium in Seattle, diasone was given to a group of 10 patients for one hundred and nineteen days without any appreciable alteration in the course of the disease as compared with a group of controls.[31] Neither the sputum nor the x-ray findings showed any benefit. Similarly, at the Chicago Municipal Tuberculosis Sanatorium, Tice and his co-workers[32] failed to note any improvement when the therapy was adequately controlled. In their tests, 29 patients with far-advanced tuberculosis were given diasone, but only 16 completed the course of therapy for one reason or another. After six months the results in the diasone-treated patients and in the controls ran parallel. Five of the former and 4 of the latter improved, whereas there were 14 unimproved treated patients and 11 unimproved controls, and 10 dead treated patients and 15 dead controls.

Both the chorioallantoic membrane of the chick embryo and the anterior chamber of the guinea pig's eye have been found to serve efficiently in the evaluation of new drugs for their possible bacteriostatic action. Thus, Steenken and his colleagues[33] showed that ocular tuberculosis in the guinea pig could be fairly well controlled and retarded in its progress by both the oral administration and the local instillation of promin. The method of eye infection offered a relatively rapid and easily observable method of testing new chemotherapeutic agents for the treatment of tuberculosis.

Twelve different alicyclic acids — chemically related to chaulmoogra oil — were tested by Emmart[34] in vitro and four were also studied in vivo (chick embryo) for tuberculostatic action. Four cyclopentyl and cyclohexyl compounds were found to be highly tuberculostatic in relatively low dosage. Emmart believes that further animal studies with these chemicals will prove profitable.

## Miscellaneous Topics

*Amyloid Disease*

Chronic suppuration, tuberculous or otherwise, usually leads to amyloid disease, which is almost universally regarded as having a poor prognosis, although the interval between the onset of symptoms and death varies considerably from patient to patient. Jacobi and Grayzel[35] recently directed attention to the therapeutic benefits of liver for such patients. In their series of 69 cases all the nontreated patients died, whereas 9 of the 16 treated patients were definitely cured and 3 others showed clinical improvement or prolongation of life. They recommend that in addition to intensive treatment of the primary infection, the patient be given 2 to 8 gm. of desiccated powdered whole liver three times daily. Since not all liver preparations are comparable in their potency against amyloid disease and since the treatment is long and costly, fresh liver may be prepared according to directions given by the authors.

The relation between amyloid disease and the necessity for surgical treatment often creates perplexing problems. To determine whether patients with amyloid disease are benefited or harmed by surgery, Auerbach and Stemmermann[36] analyzed the records of 486 cases of amyloid disease in which the diagnosis was proved by autopsy. Forty-three patients had fifty-two major surgical operations after the detection of amyloid disease, and 43 had seventy-seven operations prior to the development of this complication. On the basis of these cases, which were comparable in many respects, Auerbach and Stemmermann concluded that the decision to operate is not to be determined by the existence of the amyloid disease itself but by the possibility of controlling the underlying infection. Control of the original infection provides the patient with his best chance for recovery. The presence of amyloidosis should be an added indication rather than a deterrent, according to the authors, who also believe that with evidence of renal or other visceral impairment, surgery becomes obligatory, for although such patients are poor risks, eradication of sinuses and arrest of infection offer the only hope of escaping death.

*Tuberculous Laryngitis*

Tuberculosis of the larynx is a serious complication of a pulmonary infection and one that is notoriously difficult to treat. According to Humphries[37] treatment of tuberculous laryngitis may be regarded as being both medical and surgical. For medical therapy he recommends comforting spray and voice rest. Under surgical treatment he lists galvanocauterization, laryngoscopy, biopsy, nerve block, tracheotomy, arytenoidectomy, bronchoscopy and collapse therapy. Bronchoscopy is practically never indicated for laryngeal tuberculosis, although it plays an important role in the management of lesions deeper within the bronchial tree. Collapse therapy, by ridding the sputum of tubercle bacilli, has an indirect beneficial action on laryngeal disease. Most satisfactory of all, according to Humphries, is electrocauterization, which gave marked relief in over 90 per cent of his cases.

Myerson[38] has advanced the hypothesis that it is not the ulceration of the larynx that is responsible for the patient's pain but the secondary infection of the involved tissues by pyogenic organisms. In support of this point of view he calls attention to the fact that spraying the diseased tissues with sulfanilamide powder brings immediate relief from pain. In his treatments a powder atomizer is used to spray between 0.3 and 0.6 gm. of sulfanilamide into the larynx at each application. He has treated 60 patients in this way, with encouraging results. In 14 cases a hopeless condition became favorable following institution of therapy.

*Gastric Juice and Tubercle Bacilli*

Bacteriologic investigation of gastric juice by culture or by guinea-pig inoculation is often performed in the laboratory examination for tubercle bacilli. Yet there is some evidence that many false-negative reactions may have been obtained because of failure to inject the animals with fresh gastric juice.[39] If delay between the time the gastric juice is obtained and its inoculation into an animal is unavoidable, it is best that the specimen be neutralized before being allowed to stand. Three times more positive reactions can be obtained when the specimens are neutralized immediately than after forty-eight hours and nearly twice as many as after a twenty-four hour interval.[40]

*Vaccination*

Although vaccination against tuberculosis with BCG (Bacillus Calmette Guérin) has never been unanimously accepted, there is increasing evidence that the procedure is of value. This is particularly true in areas where tuberculosis is associated with a high mortality. An impartial evaluation of vaccination with BCG has been summed up in a concise and lucid fashion editorially.[41] In support of the thesis that vaccination provides limited protection to heavily infected groups, the six-year results of Aronson and Palmer[42] with groups of North American Indians may be cited. This report is based on the study of 1550 vaccinated Indians and 1457 controls who were resident in four widely scattered reservations. The initial testings and vaccinations were concluded in February, 1938, and the cases were followed annually until 1944. These studies showed that there were 60 deaths (from all causes) in the controls, but only 34 in the group vaccinated with BCG. Whereas 4 deaths from tuberculosis were recorded in the vaccinated group, there were 26 in the nonvaccinated. Forty cases of roentgenologically evident disease developed in the group vaccinated with BCG, and 185 cases were detected in the controls. Thus it appears that considerable benefit was obtained by this form of vaccination.

Attention was called in an earlier review[43] to the possibility of using the vole bacillus as an immunizing agent against tuberculosis. Present work with guinea pigs indicates that immunization with the vole bacillus takes place but that the degree of protection obtained is apparently no greater than that resulting from vaccination with BCG.[44]

*Expectorants*

The continuing researches of Boyd and his colleagues[45–47] are uncovering many new facts regarding the expectorant drugs. For example, they note that paregoric (camphorated tincture of opium) has been used for many years as a sedative in cough mixtures, with little investigation of its mode of action. But, by measuring the output of respiratory-tract fluid in different animals, they concluded that paregoric has considerable expectorant action, and that this action is greater than that of any of the individual components of paregoric or that obtained by a summation of the individual effects. Best results were obtained with preparations that had aged a year or longer. If the afferent vagal nerves from the stomach were severed, paregoric did not augment the respiratory-tract fluid — an indication that it acts reflexly through the stomach.

A variety of volatile oils have also been tested for their ability to stimulate respiratory-tract fluid. Of four terbinthinate oils tested, oil of turpentine proved most effective. Among the other volatile oils, oil of anise was most potent. The authors believe that if these data apply to man they indicate that oil of anise is not being used to its optimal extent as an expectorant drug. The expectorant volatile oils do not act reflexly from the stomach but rather on the secretory cells of the respiratory tract. The inclusion of several different expectorants in one cough mixture does not seem to enhance its expectorant action, as measured by respiratory-tract fluid.

*Depth Growth of Bacilli*

The growth of bacilli submerged in a liquid culture medium more nearly approximates that of the bacilli in living animal tissues than growth on the surface of a medium exposed directly to the atmosphere.[48] The technics for obtaining depth growth are described by Drea[48, 49] who also points out that this type may be used to test the effect of various substances on the growth and nutrition of the tubercle bacillus. By submerged growth technics, Dubos[50] demonstrated that certain complex lipids had a remarkably stimulating effect on the multiplication of mycobacteria. Addition to Long's synthetic medium of small amounts of phosphatides and of long-chain fatty-acid esters enabled the organisms to grow far more quickly. Thus, with submerged growth technics, testing for tubercle bacilli is becoming both more sensitive and more rapid.

*Calcifications, Coccidioidomycosis and Histoplasmosis*

The long held dogma that all calcifications within the lung are due to tuberculosis is rapidly being shattered with the discovery of the role played by other micro-organisms. Further evidence of the ability of coccidioidomycosis to produce calcifications is brought out by the studies of Butt and Hoffman,[51] who did coccidiodin tests on 1165 patients at the Santa Fe Coast Lines Hospital in Los Angeles and found that 302, or 26.0 per cent, were positive reactors. The greatest incidence of infection (62.8 per cent) was found in the group of patients coming from the San Joaquin valley. The calcifications of tuberculosis and those of coccidioidomycosis are practically identical, but in some cases the presence of apical scarring (in tuberculosis) helps differentiate the two conditions.

There is some evidence that infection with *Histoplasma capsulatum* may also be responsible for pulmonary calcifications. Palmer,[51] who explored the geographic distribution of histoplasmin sensitivity in the United States by skintesting of 10,580 nurses in eleven different cities, discovered that sensitivity varies widely in different geographic areas, from a low of 5 per cent in and around Minneapolis to a high of 60 per cent in Kansas City, Missouri. In the New England states, 10 per cent of the nurses reacted to the histoplasmin.

To determine the cause of pulmonary calcifications in children in one county in Tennessee, Christie and Peterson[53] tested 344 with tuberculin, histoplasmin and haplosporangin, and also had chest roentgenograms taken. Calcifications were found in 53.2 per cent, whereas only 21.5 per cent reacted to tuberculin. They regard this as further evidence that in many sections of the United States the prevalence of pulmonary calcifications is far in excess of that which can be explained by tuberculosis as revealed by tuberculin cutaneous testing. It is interesting to note that no child reacted to the haplosporangin, the specificity of the skin reactions thus being demonstrated. Reactions to histoplasmin were observed in 73.2 per cent. Of the group of 78 children who did not react to either tuberculin or histoplasmin, 14 (17.9 per cent) had pulmonary calcifications. Christie and Peterson conclude that present concepts of the primary complex or first-infection tuberculosis in its relation to pulmonary calcification need re-evaluation. The implications of these findings, which challenge a dogma that has existed for many years are nothing short of revolutionary.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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## CASE 32331

### PRESENTATION OF CASE

A thirty-nine-year-old mechanic entered the hospital because of a chronic cough.

Coughing episodes began twenty years before entry; they occurred about twice a year, lasting two or three weeks and producing about half a cup of greenish sputum daily. Fourteen years before entry the patient had an attack of lobar pneumonia on the left side. Seven years later the cough became chronic, with a slight increase in severity during the winter. The sputum produced was usually greenish but occasionally brownish, yellow or white. It varied in amount daily from half a cupful to two cupfuls when an upper respiratory infection was present. Repeated chest x-ray films taken by a physician were reported as showing only bronchitis.

Two years before entry the patient experienced chest pain for the first time. The pain was localized to the right infraclavicular region and persisted as a steady dull ache, but was not made worse by coughing and never interfered with sleep. Concomitantly he also developed moderate hoarseness. A year before entry the patient began to lose weight and strength and a few months later had hemoptysis. Subsequently he continued to raise a little blood-streaked sputum almost every morning. On one occasion he raised almost a tablespoonful of pure blood. Five months before entry he went to a tuberculosis sanatorium because he felt "run down." A chest film was said to have shown healed lesions at both apexes. Nevertheless he was placed on the waiting list and seven weeks before entry entered the sanatorium for observation. While there he gained 3 pounds and felt much improved, although the morning hemoptyses continued. Three weeks later the right infraclavicular pain had almost disappeared, but a similar dull, steady ache developed in the area of the sixth rib anteriorly, immediately to the right of the nipple line. In addition, there were occasional fleeting dull aches over the left chest anteriorly, localized at various points but chiefly near the apex of the heart. A chest tap attempted at the sanatorium revealed no fluid. No pneumothorax therapy was given. The patient had never had wheezing, pain on respiration, night sweats or exertional dyspnea. During the year before entry he lost 13 pounds despite a good appetite. On leaving the sanatorium he was told that he did not have tuberculosis.

Five years before entry the patient's brother, with whom he had been living, entered a tuberculosis sanatorium, where he ultimately expired.

Physical examination revealed a well developed and well nourished man in no apparent distress. The right middle and lower lobes of the lung were dull to percussion and showed diminished breath sounds and tactile fremitus. A few coarse, moist rales were heard over the same area. There was no tracheal or mediastinal deviation. The heart was normal.

The temperature, pulse and respirations were normal. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood revealed a red-cell count of 6,480,000, with 75 per cent hemoglobin, and a white-cell count of 17,650, with 81 per cent neutrophils. Repeated sputum smears were negative for acid-fast organisms.

X-ray studies of the chest revealed a mass at the right hilus within which there were several cavities measuring up to 3 cm. in diameter. In the lateral view the mass was seen to occupy the apex of the lower lobe, with the largest cavity lying posteriorly. There was no involvement of the middle and only partial atelectasis of the lower lobe. Slight scarring was seen at both apexes, and there was some thickening in the region of the right costodiaphragmatic angle.

A bronchoscopy was performed.

### DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT: To summarize, this patient had a cough of twenty years' duration that began at the age of nineteen. For the first thirteen years this cough was intermittent, occurring in episodes of brief duration and punctuated by an attack of what was said to be lobar pneumonia. During the next five years the cough became continuous and chronic, with a fair amount of sputum, but the x-ray films were said to have shown only bronchiectasis. Two years before entry a new symptom appeared — chest pain, accompanied by hoarseness. In the year before entry constitutional symptoms and hemoptysis appeared, but the x-ray findings were not diagnostic, and it can be assumed that the sputum was negative at the sanatorium. On admission, physical examination showed the patient to be in good condition, without fever, and he had what I assume to be signs of partial bronchial obstruction on the right. Again he had a negative sputum.

We might see the x-ray films at this point.

DR. JAMES R. LINGLEY: These are the cavities described lateral to the hilus in the anteroposterior view. In the lateral view they lie posteriorly in the apex of the lower lobe. The cavities are surrounded by considerable density. The whole apex of the lower lobe is involved in this process. This film was taken after tapping the chest, and there is a small amount of air in the pleural cavity, which was not present previously. The diaphragm is possibly a little elevated on the right. The heart shadow is not displaced.

DR. SHORT: Is there atelectasis of the right lower lobe?

DR. LINGLEY: I think that there is some atelectasis in the apex.

DR. SHORT: Is there also a mass in the area of the hilus?

DR. LINGLEY: A mass or an area of consolidation.

DR. SHORT: Is the mass infiltrating?

DR. LINGLEY: Its borders are not at all distinct, but perhaps that is due to atelectasis.

DR. SHORT: And you can see no definite mediastinal lymph nodes?

DR. LINGLEY: No.

DR. SHORT: There are a number of diagnostic possibilities in this case. I might consider what seem to me the unlikeliest ones first. It does not seem reasonable to explain the whole picture on the basis of bronchiectasis or any usual type of chronic pulmonary infection. One must assume that there was a lesion obstructing the bronchus to the right lower lobe, which was perhaps responsible for the distal pulmonary infection. The absence of mediastinal lymph nodes is against lymphoma with invasion of a bronchus by direct extension. Similarly there is no suggestion of extension into a bronchus from a neoplasm of a neighboring structure, such as the esophagus.

This is not the x-ray picture of sarcoid, and although an infection like actinomycosis can start in a bronchus and cause multiple cavitation, the patient would probably have been sicker, with fever and possibly chills.

Three possibilities therefore remain. The most probable at first glance is carcinoma, that is, a primary bronchiogenic carcinoma. Metastatic lesions that invade the bronchus and simulate primary carcinoma are comparatively rare, and there was no suggestion of a primary lesion elsewhere in the body. The patient had many of the cardinal symptoms of bronchiogenic carcinoma: cough, hemoptysis and dull, nonpleuritic chest pain, although he had no wheezing or dyspnea. There was a mass, if one may call it that, in the region of the right hilus. Cavitation associated with infection distal to such a growth is frequently seen. Hoarseness, not associated with a chest lesion, often indicates cancer, but in this case the lesion seems too low to involve the nerve supply to the larynx and in any event there is no record of a vocal-cord paralysis. The greatest objection to the diagnosis of primary bronchiogenic carcinoma is the duration of symptoms. The seven-year history of chronic cough seems too long, unless one assumes that the patient had a bronchiectasis of long duration, which was not connected with the lesion that brought him to the hospital. Even the more definite symptoms for two years before admission seem too long not to have produced obvious x-ray and clinical evidence of new growth.

Next tuberculosis must be considered. I meant to ask Dr. Lingley if he saw any evidence of scarring at the apexes.

DR. LINGLEY: These films, which look very clear to me, do not reveal anything definite at the apexes.

DR. SHORT: There was a family history of what was probably tuberculosis. The long duration of symptoms suggests pulmonary tuberculosis but not in the face of the negative x-ray films. The repeatedly negative sputum examinations are also against this diagnosis. More than one case of bronchial tuberculosis in this hospital, however, has been diagnosed by bronchoscopy after a negative sputum examination. Still I am forced to reject this possibility and to consider the tuberculosis in this case confusing rather than contributory.

A third possibility is benign tumor of the bronchus. By far the most frequent is the so-called "benign adenoma," which usually occurs in younger people than those with primary carcinoma. Although benign adenoma may be locally invasive and is believed by some to go on to actual malignancy, it grows slowly and is not prone to metastasize. I might mention that in benign adenoma large hemoptyses, with free intervals, are more usual than the repeated slight hemoptyses that this patient had. As an explanation of the cough, I can picture such a tumor's causing long continued irritation and then enlarging to the point of causing bronchial obstruction and distal infection. Perhaps by the time the patient entered the hospital the lesion was actually locally invasive. The relatively good condition of the patient, as well as the symptomatic remission in the sanatorium, is in favor of this diagnosis. I do not believe that a definite diagnosis can be made without the aid of bronchoscopy, but in the light of the whole history benign adenoma presents fewer objections than any other diagnosis.

DR. DONALD S. KING: Would you change the diagnosis if you knew that there was one positive sputum examination at the sanatorium?

DR. SHORT: That might influence me slightly.

### CLINICAL DIAGNOSIS

Carcinoma of lung.

### Dr. Short's Diagnosis

Adenoma of bronchus.

### Anatomical Diagnosis

**Epidermoid carcinoma of bronchus (Grade III).**

### Pathological Discussion

Dr. King: This was an interesting case. The patient entered Middlesex County Sanatorium with a diagnosis of pulmonary tuberculosis. There was a positive family history in the case of the brother, and the early x-ray films of the patient showed a lesion in the right upper lobe that was not visible in the films displayed here. The lesion at the right hilus, which was seen in these films, was not present when he was first admitted to the sanatorium but was demonstrable after a four-month period, during which moist and musical rales over the right mid-chest in front also developed. The signs and the x-ray findings were observed at the time when Dr. Lowrey Davenport was first looking for indications for bronchoscopy in patients with tuberculosis at the sanatorium, and this was the first patient whom he bronchoscoped there. The findings were so striking that he had no difficulty in selling the procedure to the sanatorium doctors in later cases. In this case the tumor mass was so large and friable that a large section was actually coughed into the bronchoscope at the time of its introduction.

Do you want to divulge the diagnosis that was made on that bronchoscopic specimen, Dr. Mallory?

Dr. Tracy B. Mallory: The tumor was a highly malignant carcinoma, probably epidermoid in type.

Dr. King: Because of this finding, a total pneumonectomy was performed. I believe that, so far as the records of the Massachusetts General Hospital are concerned, this is one of two patients who are now living five years after a removal of a lobe or entire lung for bronchiogenic carcinoma. The patient has been under observation in the hospital recently because of an acute infection in the remaining lung. He recovered satisfactorily.

Dr. Mallory: He now has survived nine years.

Dr. Short: Were there positive lymph nodes in the hilus?

Dr. Mallory: No. The tumor was at the junction of the middle-lobe and the lower-lobe bronchus. It was an ulcerated lesion, nearly 2 cm. in diameter, and the histologic appearance was that of a highly malignant tumor. This is the last case on which I should have given a favorable prognosis, and strangely enough the patient presents our best result.

Dr. King: Perhaps the fact that the diagnosis was made the sigearly is nificant point in this case. The symptoms, signs and x-ray findings were discovered at an early date, because he was in the sanatorium during this period.

Dr. Short: You assume that the previous symptoms were due to tuberculosis?

Dr. King: I do not know just how many of the symptoms were due to tuberculosis, but I had understood that the surgical specimen showed not only cancer in the right lung but also a tuberculous cavity. We have therefore always spoken of this case as a combination of both tuberculosis and carcinoma. I may be wrong in my memory of the pathologist's report on the surgical specimen.

Dr. Mallory: We have no record of tuberculosis.

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## CASE 32332

### Presentation of Case

*First admission.* A forty-three-year-old Chinese laundryman entered the hospital because of persistent cough with hemoptysis.

The history was not easy to obtain, because of language difficulties. The patient was apparently well until a year and a half before admission, when for the first time he coughed up about a cupful of blood. Subsequently he continued to have hemoptyses at irregular intervals varying from one to several weeks. The cough was worse in the morning, during the winter months and in the presence of upper respiratory infection. Occasionally it was accompanied by a sharp pain in the left epigastrium. The appetite became poor, and during a period of four months the patient lost about 8 pounds. There was no weakness or fatigue. Fifteen months before admission, the patient was seen in the Out Patient Department. An x-ray film of the chest at that time revealed increased density in the region of the lingula and both lower lobes. The left lower lobe appeared to be nearly completely collapsed in the basilar segment, but the dorsal division did not seem to be involved. Within the collapsed lobe there were dilated bronchi. There was also beginning dilatation of the lateral division of the lingular bronchus of the left upper lobe and of the anteromedial bronchi of the middle lobe, as well as the anterior division of the right lower-lobe bronchus. Bronchoscopy showed moderate hemorrhagic bronchitis of the left lower lobe, with questionable bronchiectasis. Repeated sputum smears were negative for acid-fast organisms. Twelve months before entry, the patient entered a state hospital because of the continued cough and hemoptyses. He remained there until his admission to this hospital. Serial sputum examinations had shown no tubercle bacilli.

The patient gave no history of tuberculosis or exposure to it. He had had an attack of "pneumonia" as a young man.

Physical examination revealed a well developed and well nourished man in no acute distress and coughing only infrequently. The sputum, however, was foul and contained frothy blood-tinged material. Percussion of the chest revealed some dullness at both bases posteriorly and slight dullness below the right axilla. There were coarse rhonchi in the right upper chest posteriorly and also a few on the left. Breath sounds seemed slightly diminished over the right chest anteriorly and laterally. The heart and abdomen were normal. The tendon reflexes of the left arm were somewhat hyperactive, and there was some weakness and flabbiness of the left hand. The fingers of both hands showed early clubbing.

The temperature, pulse and respirations were normal. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood showed a red-cell count of 4,600,000, with 11.3 gm. of hemoglobin, and a white-cell count of 6600, with 71 per cent neutrophils and 19 per cent lymphocytes. The total protein was 8.2 gm. per 100 cc. The urine was normal.

X-ray examination of the chest, including bronchograms, showed no change from the previous findings, the most marked bronchiectatic process being in the left lower lobe.

The patient was discharged on a high-protein diet.

*Second admission* (three weeks later). The patient was readmitted for surgery. Since discharge he had continued to cough up daily about 100 cc. of foul, gray sputum, but there had been no further hemoptyses. Physical and laboratory findings were essentially the same as on the previous admission. The patient was placed on aerosol penicillin to reduce the amount of sputum. On the fourteenth hospital day an operation was performed.

## Differential Diagnosis

Dr. Reed Harwood: The diagnosis in this case involves a discussion of the causes of bronchiectasis. Bronchiectasis may be defined as a chronic progressive disease of the bronchi, with bacterial invasion of the bronchial wall and the surrounding lung tissue. It results in an inflammatory reaction of the bronchial wall, dilatation of the bronchus and varying degrees of inflammatory reaction and fibrosis of the adjacent lung. Different sorts of mechanical forces are said to account for the bronchial dilatations. For example, in the presence of obstruction of a bronchus, coughing increases not only the intrabronchial pressure distal to the obstruction but also the difference between the intrapleural and the intrabronchial pressure with each inspiration. It is believed that most cases of bronchiectasis are caused by obstruction of the involved bronchus as well as by infection. The infecting organisms may be any of the pyogenic bacteria, as well as spirochetes and fusiform bacilli, the tubercle bacillus and other less frequent organisms. The usual sequence of events in the development of bronchiectasis is repeated attacks of bronchitis, often associated with chronic sinusitis. Unresolved pneumonia or repeated attacks of bronchopneumonia may also initiate the process. In the case under discussion it seems probable that the bronchiectasis had its beginning when the patient had pneumonia as a young man. The history of chronic cough, which was worse in the morning, during the winter and during respiratory infections, is typical, as is the character of the sputum, the periodic hemoptyses and the clubbing of the fingers. Indeed, there is little in the record to suggest that this case does not fall into this category. I believe that the patient was prepared for left lower lobectomy with this diagnosis in mind.

Some of the other conditions that cause bronchiectasis must be considered. Tuberculosis was obviously suspected in this case. Repeated failure to find tubercle bacilli in the sputum is strong evidence against this diagnosis. It is extremely probable that while the patient was at the State Hospital the stomach contents were examined for tubercle bacilli. Tuberculosis most frequently involves the apexes of the lungs, but its absence in these areas does not exclude it from consideration. A tuberculous ulceration of the lower main-stem bronchus, however, would probably have produced a rapid spread of the disease and a downhill course. A tuberculous stenosis in this region would have been visible to the bronchoscopist. The involvement of bronchi going to several lobes is against a localized tuberculous lesion.

Could a tumor have caused the bronchiectasis? Benign and malignant intrabronchial tumors cause obstruction to the bronchus with infection beyond the obstructed area, as do tumors of mediastinal lymph nodes and infected lymph nodes. One would expect, however, to find the bronchiectasis confined to the involved segment. Besides, the bronchoscopist would be able to see the obstructed area. The same reasoning applies to the presence of a foreign body in the bronchus.

Much rarer causes of bronchiectasis are actinomycosis and other mycotic infections. I assume that the presence of sulfur granules or yeast cells would have been detected in some of the many sputum examinations. In actinomycosis the constitutional symptoms are apt to be severe, and there is a tendency to sinus formation and particularly to abscesses that drain through the chest wall.

Mention is made of increased reflexes in the left arm, with weakness and flabbiness of the left hand. Without more precise neurologic findings, it is difficult to connect this observation with the pulmonary disease, especially since the lesions in the lung were too low to have produced symptoms of brachial plexus. Metastases of tumor could, of course, account for such a finding, but I do not consider the data sufficient to make a definite diagnosis.

In summary, I believe that this patient had bronchiectasis as a result of repeated upper respiratory and bronchopulmonary infections. Tuberculosis is my second choice, but there is little evidence to support this diagnosis. The diagnosis of tumor or other unusual causes of bronchiectasis remains in the realm of speculation.

### Clinical Diagnoses

Bronchiectasis.

### Dr. Harwood's Diagnosis

Bronchiectasis of left lower lobe.

### Anatomical Diagnoses

**Bronchiectasis of left lower lobe.**
Pulmonary tuberculosis.

### Pathological Discussion

Dr. Tracy B. Mallory: This patient was operated on with a preoperative diagnosis of bronchiectasis, as Dr. Harwood suggested, and a lobectomy was done. The presence of extensive bronchiectasis was confirmed, but no obstruction of the major bronchi was found. There was a marked chronic inflammatory process in the lung parenchyma as is often present in cases of bronchiectasis, and the one surprise was that scattered through this inflammatory tissue were nodules of tuberculous infection. Most of these were fairly well healed, but one or two still had frankly caseous centers, a few giant cells and some probable degree of activity, although I am inclined to believe that the tuberculosis was coincidental and not responsible for the primary lesion, which was certainly bronchiectasis.

Dr. Donald S. King: You have not often found tuberculosis in lobes that have been removed?

Dr. Mallory: Very seldom indeed.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

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Material should be received not later than noon on Thursday, two weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## STATUS OF NATIONAL HEALTH LEGISLATION

The stormy seventy-ninth session of Congress has terminated without the enactment of proposed health legislation, which has been surrounded with controversy and recrimination since the first committee hearings. Proponents of the Wagner–Murray–Dingell Bill have postponed their efforts to obtain enactment until Congress reconvenes in January, 1947; and the Pepper Bill has not been reported out of committee.

A respite is thus granted in which the medical profession can marshal its forces for the fight when these bills come up for consideration during the eightieth session of Congress. Organized medicine also has an opportunity to initiate action that will make the threatened legislation unnecessary.

Senate Joint Resolution No. 177, introduced by Senators Pepper and Taft on instructions from the Senate Committee on Education and Labor, fills a need that has been greatly felt and also demonstrates what may be a healthy trend away from the type of governmental control and participation embodied in the Wagner–Murray–Dingell and Pepper bills. The resolution amends the Social Security Act to provide for increased grants to the states for crippled children, maternal and child health and child welfare; favorable action on the resolution — which has still to be considered by the Senate Finance Committee and the House Appropriations Committee — would establish over the funds concerned regulations and controls similar to those already in effect on appropriations for the Children's Bureau. Legislation that takes the form of badly needed aid for existing welfare agencies — rather than that of creating a spate of new bureaus and extending regimentations and control to fields that should be beyond the concern of the Government — is always welcome.

Another encouraging note is provided by Senate action on President Truman's reorganization plan, which transfers the Children's Bureau from the Department of Labor to the Federal Security Agency and thus affords an opportunity for co-ordination between the Bureau and the United States Public Health Service and similar agencies.

## NEW ANTIMALARIAL DRUGS

During the past eight months, the discovery of two new antimalarial drugs has been announced. One, called "paludrine" (M 4888), was produced in England,[1, 2] and the other SN 7618, which was later called "chloroquine," was developed in this country and announced by the Board for the Co-ordination of Malarial Studies.[3, 4] Both drugs are the result of extensive efforts on the part of British and American scientists during World War II to find new chemotherapeutic agents for the prophylaxis, suppression and treatment of malaria.

The initial and urgent need for an extensive research program on the chemotherapy of malaria arose out of the grave problem of malaria control and treatment among the armed forces in World War II. The loss of the main source of cinchona bark for the production of quinine and the questionable value of quinacrine (Atabrine) furnished the driving force for research into the fundamental facts about malarial parasites, the disease that they produce and the chemotherapy of the disease. The achievements and value of the program are now becoming apparent.

Aside from the fundamental information that helped define the problems involved in suppressing and curing malaria, over fourteen thousand compounds were tested for their activity against avian malaria in this country and eighty of these compounds were subsequently tested on cases of human malaria. In addition, over one thousand compounds were made and tested in England.[5]

Coincident with this vast search for new effective drugs, experimentation with quinacrine proved that different dosage schedules, employing larger doses, were needed to produce and maintain effective plasma levels for suppression and treatment.[6] This information helped to explain previous difficulties with the drug. The new dosage schedules caused a dramatic reversal in the trend of malarial incidence among the armed forces. Malaria could be suppressed, and a radical cure of falciparum malaria could be effected, but quinacrine continued to fail as a true casual prophylactic and as a radical cure for relapsing vivax malaria, particularly with strains of Pacific origin. Although the new quinacrine therapy was of strategic value in winning the war, the search for more effective drugs continued.

The reasons for the failure of quinacrine and quinine to produce radical cures of vivax malaria and to prevent the relapsing nature of the disease in a majority of cases are slowly becoming understood. These drugs are effective against all stages of the parasites in the blood stream, but they are apparently unable to penetrate other cells and thus to sterilize the more or less hypothetical tissue stage of the plasmodia. These tissue stages, which develop from the sporozoites injected by the infective mosquitoes prior to invasion of the blood stream and the erythrocytes, have been seen and studied in several types of avian malaria.[7] The experiments of Fairley[8] and his collaborators suggest that they also exist in human malaria. Thus an effective drug must presumably penetrate selectively and exert a lethal effect on the parasites within the cells of such organs. This process appears to be necessary for true casual prophylaxis, radical cure and the prevention of relapses.

With the above information, the English scientists decided to explore some new ring system that would satisfy the requirements for antimalarial activity against the tissue stages of the parasites.[9] Compounds known as pyrimidines were chosen for the initial studies because of their physiologic importance in the synthesis and function of cell nuclei. That this choice was a fortunate one was soon verified by the discovery of antimalarial activity in a derivative of anilinopyrimidines called "2666."

The evolution of paludrine from 2666 is an exciting account[9] and a prime example of the type of achievement made possible by a closely co-ordinated collaboration between scientists from different fields. It is sufficient to say here that paludrine is $N_1$-p-chlorophenyl-$N_5$-isopropyl biguanide and that the compound is "a chemical type not hitherto met with in chemotherapy."[5] The antimalarial activity of this drug initially demonstrated in cases of human malaria in England has been substantiated by field

**MASSACHUSETTS MEDICAL SOCIETY**
**POSTWAR LOAN FUND**

**The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:**

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trials at Cairns, Australia.[10, 11] The drug has been shown to be a true casual prophylactic and to produce a radical cure of malignant tertian malaria. With vivax malaria, paludrine is a partial casual prophylactic; tests regarding radical cure were not completed, but a dosage of 0.1 gm. twice a week appeared to prevent relapses indefinitely. Furthermore, the difference between the therapeutic and the toxic dose was found to be great enough to permit a wide latitude in therapy without danger to the patient.

Although detailed accounts about the discovery and therapeutic trials of chloroquine have not appeared, the story of this new antimalarial drug is probably just as fascinating. Here again, falciparum malaria is cured radically but vivax malaria is more resistant to treatment. The primary attributes appear to be the small dosages that are effective in producing radical and clinical cures; it has approximately three times the antimalarial activity of quinacrine and causes no discoloration of the skin.[4] Since this drug has been tried on over 5000 cases of human malaria, judgment concerning its efficacy rests on firmer ground than does that for paludrine. Reports of well controlled field experiments comparing the simultaneous effects of the two drugs will, however, be awaited with great interest.

Those who know the malarial problems awaiting control and eventual solution are well aware that the existence of two new drugs cannot achieve the desired results. The combined efforts of governments, peoples and specialists in malariology utilizing drugs, antianopheline campaigns and new insecticides are needed for effective malaria control.

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## MASSACHUSETTS MEDICAL SOCIETY

### DEATH

MESERVE — Faith L. Meserve, M.D., of Weston, died July 19. She was in her fifty-second year.

Dr. Meserve received her degree from Boston University School of Medicine in 1926. She was a fellow of the American Medical Association.

Her mother, two sisters and a brother survive.

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## MISCELLANY

### DR. JOHN E. FISH — AN APPRECIATION

Massachusetts has long taken pride in its pioneering leadership toward social improvement and cultural achievement. Here in Massachusetts John Harvard founded the first college. In later generations, Horace Mann fathered public-school education as it is known today; Dr. Samuel Howe organized the Perkins Institute for the Blind; and Laura Bridgman and Helen Keller, without sight or hearing, gained liberal educations. In line with these traditions, the excellent St. Botolph Street School for Crippled Children was founded for the purpose of extending education to children whose physical disabilities prevented their attending the regular schools. It soon became apparent, however, that a day school could not meet the full requirements for educating all the cripples in the Commonwealth. In 1904, the Massachusetts Legislature therefore created a novel institution to serve as a public boarding school, with hospital facilities available to all disabled children, whether rich or poor.

The opening of the Hospital School was delayed for four years while land was purchased and the first buildings erected. During this interval, one of the greatest difficulties had been to find a man qualified to serve as superintendent. In 1908, by rare good fortune, the trustees selected Dr. John E. Fish for this difficult post, and nowhere could they have found a man better qualified for these new and untried duties. Born in Vermont, the son of a country doctor, he was already steeped in the fine traditions of the medical profession, to which he added his own liberal education at Dartmouth College and Medical School. He had gained administrative experience in some of the state institutions and had acquired a clear insight into human character through the patients he dealt with there. More fortunate still, Dr. Fish was blessed with a wife ideally suited to help in the life of such a school as this. She was the daughter of a Civil War surgeon who spent his later years in family practice in Vermont. With her refinement, quiet humor and unfailing cheerfulness, she brought to her husband the help that a man needs most under difficulties. Thus Dr. Fish was the perfect choice in every respect, to face the unforeseen problems and difficulties of the new institution. Time has tried him for thirty-eight years, during which he has carried the school through good times and bad, through the upheaval of two world wars and into the second postwar era. Without a break in his long service, he has been reappointed by governors of both major political parties. He has outlived the members of the original Board of Trustees who founded the school and has served under the chairmanship of the son of one of them; the sons of three of the doctors on the earlier consulting staffs have taken the places of their fathers beside him. From the beginning and without faltering, he has fulfilled and advanced the highest hopes of those who first conceived of the institution. As one of the present trustees has remarked: "The school was merely a dream when it was planned. Fish has made that dream come true."

The extent of his achievement in giving reality to such a dream can be measured only by the lives it has liberated from crippled helplessness into the freedom of self-supporting and educated citizenship. It is difficult to appreciate the neglect of educational opportunities for handicapped children during the early years of this century. In the beginning, the school's admissions included many children who had grown into adolescence without a single day's schooling. At the age of fourteen and fifteen, these boys and girls were given their first lessons in elementary reading and writing. Every form of disability was represented among the applicants, but no

matter how completely helpless the child appeared physically, none were denied the opportunities of learning provided they had the capacity to understand. One girl, who was born without hands went to the school at the age of four. After graduation from the eighth grade, she took a stenographic course and learned to write shorthand at a rate of one hundred and twenty words a minute. She has gone on to the study of art and has painted some creditable portraits. This girl is only one of the many whose physical handicaps would have seemed totally disabling in any other locality but whose development at the school has been possible. They came as children with useless limbs and twisted backs, or confined to crutches and wheel chairs or with halting, unbalanced gaits or perhaps unable to get off a litter. But they acquired the spirit of strength and independence, the will to do for themselves, and they left equipped with knowledge equivalent to that of any normal children in similar grades. In all, there have been six hundred and forty-one graduates of the school, a large number of whom have become self-supporting and many of whom are raising and supporting their own families. Most of them have found specialized jobs of one type or another. Some, however, have carried their education on into further fields. Thus, two have won seats in the Legislature, two are artists, two are lawyers, one a doctor, another a nurse and still another a social worker. Seven of them have returned to serve on the staff of the school — one as treasurer, and one as head of the school department. Seven outgrew their physical handicaps and served in the armed forces during the war.

Three general ideas that have formed the basis of Dr. Fish's program can best be described by quotation of his own terse phrases. The first of these is the declaration, "Education of a crippled child is not a charity any more than the education of a normal child." One might say that such a statement seems self-evident; yet it was not always so regarded, nor has any state in the Union other than Massachusetts gone to such lengths in giving this thought practical fulfillment. In the early years of the school, a well meaning critic once objected that money spent on the education of a crippled child would be wasted unless the child could be made self-supporting. To this objection, one of the school's founders replied: "That is not the way our Saviour looked at it. He said, 'Give life, and give it more abundantly.' " Throughout his career, Dr. Fish has clung to that doctrine, and it is suitably inscribed on the memorial clock tower that the graduates have dedicated to him.

As a second principle, Dr. Fish believes, "No form of surgical care or other treatment can be regarded as complete that neglects the social, moral and mental growth of the child." This statement clearly exposes the most serious defect in other programs for crippled children: too many private, state and federal institutions offer only operative or postoperative surgical treatment, not recognizing that partial correction of a physical deformity still leaves a crippled mind and not realizing that in the months, and often the years, spent in clinics and hospital wards and convalescent centers, the child loses invaluable time both from textbook lessons and from character-building experience. Such lessons and such experience must come early enough to help the child develop the right mental attitude; if they are postponed too long, the damage to the child's mental processes may be irreparable. As the trustees observed in their first report: "Disabled children who have been too tenderly cared for much beyond the age of puberty are liable to develop a lack of initiative and indolence that is difficult to overcome. A pauperization of character has been developed." The ideal of the Hospital School has therefore been to allow education, surgical care and convalescence to proceed together — and note that education is given first place.

Perhaps the most important basis of the school's success is explained in Dr. Fish's third and vital maxim, "It has been found that the placing of crippled children under healthful conditions, thus directly stimulating opportunities for play, study and amusement, tends to destroy any source of self-pity and teaches them to minimize or forget their disabilities." By this concept, the role of education is extended beyond ordinary schoolbook instruction and reaches a personal, psychologic, almost spiritual perspective. It aims at improving character, so that these children may grow to a richer, more self-sufficient maturity. That, essentially, is what the Hospital School has succeeded in doing with the invalids who are enrolled as students. For the fulfillment of this purpose, it was recognized that even crippled children are dominated by normal cravings for games and social activities, and that such activities constitute a necessary part of their development. There is not space to describe the numberless methods, large and small, that Dr. Fish employed to carry his thought into action. One example will serve to illustrate the rest. This was the organization of a baseball team on which each boy was allowed to play so far as his own abilities permitted. The legless pitcher, who trained himself to strike out normal boys of the local schools, will always be remembered, as will the batter with artificial legs who was supplemented by an armless boy running bases. No matter how the score stood with their rivals, such teams defeated their own disabilities, which were their real opponents. The same principle was carried to all the school's activities. Musical talents were cultivated by choir singing and by the organization of a school band. A shop for watch repairing under the tutelage of an expert craftsman has been eagerly attended. The dormitories were made as home-like as possible, and the girls were encouraged to help in cooking and serving meals. The girls of the senior class were given a beautifully furnished reception room, where they served afternoon tea once a week to guests and callers. The local clergy have co-operated, and Catholic, Protestant and Jewish services are held at the school every week. Thus, so far as possible, the children learn to lead normal lives in an optimistic, healthful and happy environment.

Based on these principles, the Hospital School has become a permanent institution in the life of the Commonwealth. It is still unequaled and unrivaled anywhere else in the world. Its traditions are now so well established that one can look forward to another generation of service on a level with what it has already produced. Now, as he retires from his duties, one feels more keenly than ever gratitude and appreciation for Dr. Fish's high-minded vision and for the devoted service and strong and wise leadership that made a dream come true.

C. H. B.

## NOTICES

### ANNOUNCEMENTS

Dr. H. Myer Bloomenthal announces his return from military service and resumption of practice of medicine and surgery at 1396 Commonwealth Avenue, Boston.

Dr. Leon Ryack, having returned from military service, announces the opening of his office for the practice of medicine at 1755 Beacon Street, Brookline.

Dr. Maurice M. Tolman has returned from naval duty and will resume the practice of dermatology at 636 Beacon Street, Boston.

### AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination (Part I) of the American Board of Obstetrics and Gynecology for all candidates will be held in various cities of the United States and Canada on Friday, February 7, 1947, at 2:00 p.m. Candidates who successfully complete this examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the Secretary by November 1, 1946. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

A number of changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Chicago from May 5 to May 11, 1946. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept a nine-month residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration (April 1, 1946).

Applications are now being received for the 1947 examinations. Final examinations will be held in Pittsburgh June 1 to 7, 1947. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

(*Notices continued on page xv*)

NOTICES (*Continued from page 238*)

## SOCIETY MEETINGS AND CONFERENCES

### Calendar of Boston District for the Week Beginning Thursday, August 22

Friday, August 23

*10:00 a.m.-12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

Tuesday, August 27

*12:15-1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

Wednesday, August 28

*10:30-11:30 a.m. Medical Clinic. Isolation Building Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

March 15-September 15. Boston University Course for Discharged Medical Officers. Page 240, issue of February 14.

September 4-7. American Congress of Physical Medicine. Page 616, issue of May 2.

September 30-October 3. Industrial Health Congress. Page 206, issue of August 8.

October 6-12. Interamerican Congress of Cardiology. Page xix, issue of June 6.

October 7-12. Seminar in Legal Medicine. Page 206, issue of August 8.

October 7-18. New York Academy of Medicine. Page 544, issue of April 18.

February 7. American Board of Obstetrics and Gynecology. Page 238.

April 28-May 2. American College of Physicians. Page 206, issue of August 8.

### District Medical Society

PLYMOUTH

October. Jordan Hospital, Plymouth.
November. Plymouth County Hospital, South Hanson.
January. Brockton Hospital, Brockton.
February. Moore Hospital, Brockton.
March. Goddard Hospital, Brockton.
April. State Farm, Bridgewater.
May. Lakeville Sanatorium, Lakeville.


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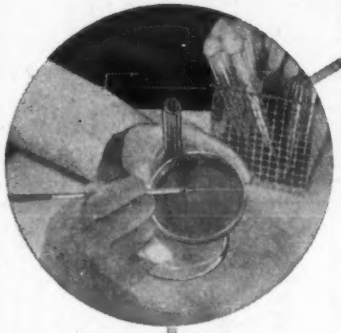

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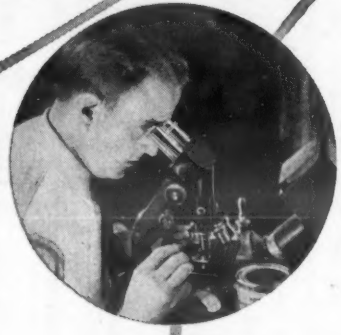

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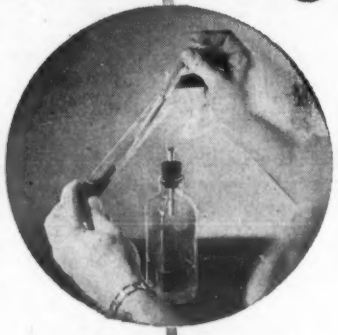

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